Uttar Pradesh Journal of Zoology

Volume 45, Issue 9, Page 8-19, 2024; Article no.UPJOZ.3404
ISSN: 0256-971X (P)

Meta-Analysis of Association of SNP 19 In-del Polymorphism at the CAPN 10 Gene with Type2 Diabetes Mellitus

Kali Charan Mishra [a] and Parul Banerjee [a*]

[a] University Department of Zoology, LN Mithila University, Darbhnaga, Bihar, India.

Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

Article Information

DOI: 10.56557/UPJOZ/2024/v45i94017

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://prh.mbimph.com/review-history/3404

Original Research Article

Received: 02/02/2024
Accepted: 06/04/2024
Published: 11/04/2024

ABSTRACT

The CAPN 10 gene encoding the larger subunit of the ubiquitously expressing calpain protein has been found to play a role in the incidence of Type2 diabetes mellitus (T2DM). Several intronic polymorphisms of the CAPN10 gene and the linked haplotypic combinations have been implicated in T2DM. The SNP 19 locus of the gene lying within intron 6 exhibits an in-del polymorphism and has been found to be associated with T2DM in several studies. However, the results have not been constant.

Keeping this in view, the present work was carried out to understand the association of the intronic SNP 19 in-del polymorphism at the CAPN 10 gene with T2DM through meta-analysis of the case-control studies. All statistical tests based on PRISMA and PROSPERO were performed on R studio (4.2.3). However, the pooled odds ratio (OR) estimates did not reveal any significant association between polymorphism at the SNP 19 locus of CAPN 10 gene and T2DM.

Therefore, it is concluded that polymorphism at the SNP19 locus of CAPN 10 gene alone has no role to play in the etiology of T2DM.

**Corresponding author: Email: parulputul@gmail.com;*

Keywords: T2DM; CAPN 10 gene; SNP polymorphisms; Case-control association studies; SNP 19; in-del polymorphisms.

1. INTRODUCTION

The calpains are a family of ubiquitous calcium-dependent cysteine proteases. They are heterodimers consisting of a small subunit which is invariant and a variable larger subunit. The larger catalytic subunit having four domains is encoded by the CAPN 10 gene. This larger subunit is unusual in the sense that it lacks the calmodulin-like calcium-binding domain and instead has a divergent C-terminal domain. This gene is located within the NIDDM1 region in chromosome 2 (2q37.3)[1]. There are several polymorphisms and haplotypic combinations within the gene which have been associated with type 2 or non-insulin-dependent diabetes mellitus (NIDDM). In fact, this is the first gene implicated in T2DM [2].

The CAPN10 gene comprises 15 exons and 14 introns and encodes a 672 amino-acid intracellular protease that has been known to play myriad roles such as Glucose metabolism, pancreatic β-cell function, regulation of thermogenesis, insulin secretion, insulin resistance etc [3–8]. Of all the polymorphisms implicated in T2DM, SNP-19 (rs3842570), located in intron 6 stands out, as it involves not a single base transition or transversion but an insersion/deletion (in-del) polymorphism having 2/3 32 bp repeats (2R/3R). A 32 bp insertion/deletion in any exon would have meant a frameshift. However, since the in-del lies in an intronic region, its implications may not be very huge. Nonetheless, SNP 19, like the other common intronic variants such as SNP 43 (rs3792267), SNP 44 (rs2975760) and SNP 63 (rs5030952) etc. have been known to alter CAPN10 mRNA expression eventually leading to insulin resistance and in many instances development of T2DM.

However, even with the huge number of studies done, the association of this in-del polymorphism with T2DM is not clear as the results are conflicting. Keeping this in view, we thought it pertinent to carry out a meta-analysis of all the case-control studies done so far so that the pooled results could take us to a conclusion as regards the role of this particular polymorphism in causing T2DM or protecting against it.

2. MATERIALS AND METHODS

2.1 Study Design

The meta-analysis was designed according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) and the published PROSPERO research protocol [9,10].

2.2 Keywords Used and Literature Databases Employed

"Type 2 Diabetes Mellitus" OR "insulin independent diabetes mellitus" OR "Noninsulin-Dependent Diabetes Mellitus" and "CAPN10," OR "Calpain 10" were used as keywords in different combinations and without filter to look for germane papers in Pubmed, Web of Science and Scopus.

2.3 Eligibility Criteria

The following inclusion and exclusion criteria were used while screening:

Inclusion criteria:

- Case–control studies conducted on any human population and assessed for association between SNP 19 polymorphism of CAPN 10 gene and risk of T2DM.
- Cases: individuals with T2DM, Controls: Individuals without T2DM.
- Allele or genotype frequencies of SNP 19 polymorphism clearly mentioned and sufficient for the calculation of odds ratios (ORs) with the corresponding 95% confidence intervals (CIs) of the polymorphism in both the case and control groups.
- Full texts available.

Exclusion Criteria:

- Reviews, meta-analysis, letters, editorial, comments, and conference abstracts.
- Family based association studies.
- In vitro, ex vivo or animal studies
- Studies lacking sufficient data on allele frequencies or data through which the respective genotypic frequencies could not be calculated.

- Studies with CAPN 10 SNP19 polymorphism as a part of haplotype analysis.
- Duplicate publications and redundant studies of duplicated data.

2.4 Screening Strategy

Initially all literature extracted from the three databases were checked for duplicates and save for one copy, the extra copies of any paper were removed. Thereafter, the titles were screened, followed by the abstracts by a group of two individuals. The steps were repeated by a group of two other researchers to be sure about the included and excluded articles.

The articles remaining after exclusion based on titles and abstracts were read thoroughly by each researcher and articles which did not meet the inclusion criteria were excluded.

2.5 Quality Assessment

The quality of each of the included study was assessed with the help of the framework laid by The Newcastle–Ottawa Scale (NOS) [11]. The scale ranges from zero to nine. Studies with a rating of 7–9 ware presumed to be of high quality, 4–6 as moderate quality, scores 4 or less ware classified as low-quality studies [12].

Quality assessment was conducted by both the authors independently. Any disagreement was sorted out by discussions between the two and if it still persisted, another expert from the field got involved to arrive at a consensus.

2.6 Data Extraction

The following facts were extracted from the included studies:

a. First author's names and year of publication
b. Region where the study was conducted or ethnicity of participants
c. The number of cases and controls
d. Genotyping method
e. Data on genotypic frequencies of CAPN 10 SNP 19 polymorphism of both cases and controls.

The extracted data was rechecked by two individuals having expertise.

2.7 Genetic Models

The SNP 19 locus exhibits an in-del polymorphism denoted as 3R and 2R respectively. While 2R is the minor allele, 3R is the major one. Therefore, the following allele(s) /genotype(s) were denoted as events vs total in the different genetic models:

a) Allele model (2R vs. 2R+3R)
b) Homozygote model (2R2R vs. 2R2R +3R3R)
c) Heterozygote model (2R3R vs. 3R3R+2R3R)
d) Additive model (2R2R vs. 2R2R+2R3R)
e) Dominant model (2R2R + 2R3R vs. 2R2R+2R3R+3R3R)
f) Recessive model (2R2R vs. 2R2R+ 2R3R + 3R3R)
g) Co-dominant model (2R3R vs. 2R2R+ 2R3R+3R3R)

2.8 Calculations of Odds Ratio (OR) and Test of Heterogeneity

R Studio (4.2.3) was employed for carrying out all statistical tests. Common Effects Model (CEM) and Random Effects Model (REM) were used to calculate the pooled OR estimates. Cochran Mantel Haenzel method was used for CEM (Mantel and Haenszel, 1959), whereas, Inverse Variance method was used for REM. Cochrane Q-test index was used for determining heterogeneity between the results of the primary studies. The I^2 values of 25%, 50%, and 75% being low, moderate, and high estimates, respectively [13]. Also, Galbraith's test was done to single out potential sources of heterogeneity in case significant heterogeneity was detected [14].

2.9 Subgroup Analysis

Ancestry and ethnicity are important parameters in population genetics. Therefore, subgroup analysis was also done based on ancestry categories. Ethnicity/ancestry was categorized as South Asian, Middle Eastern, Mexican and Hispanic, European, African Descent and East Asian. This was according to the classification of Morales et al. [15]

2.10 Publication bias

Begg's funnel plot was used to check for publication bias. This was also followed by Egger's test to check funnel plot asymmetry [16].

3. RESULTS

3.1 Included Studies

The total number of studies identified was 4,265 (188 from Pubmed, 2171 from Scopus and 1906 from Web of Science). 244 duplicate articles were excluded while 4021 studies were included for the next level of screening. Out of these 4021 studies, 3973 articles were excluded during the screening of titles and abstracts. The full texts of all the 48 articles left were studied thoroughly. 18 studies could not be included as they did not meet the inclusion criteria. Therefore, finally data from 30 studies were used for meta-analysis (Fig. 1).

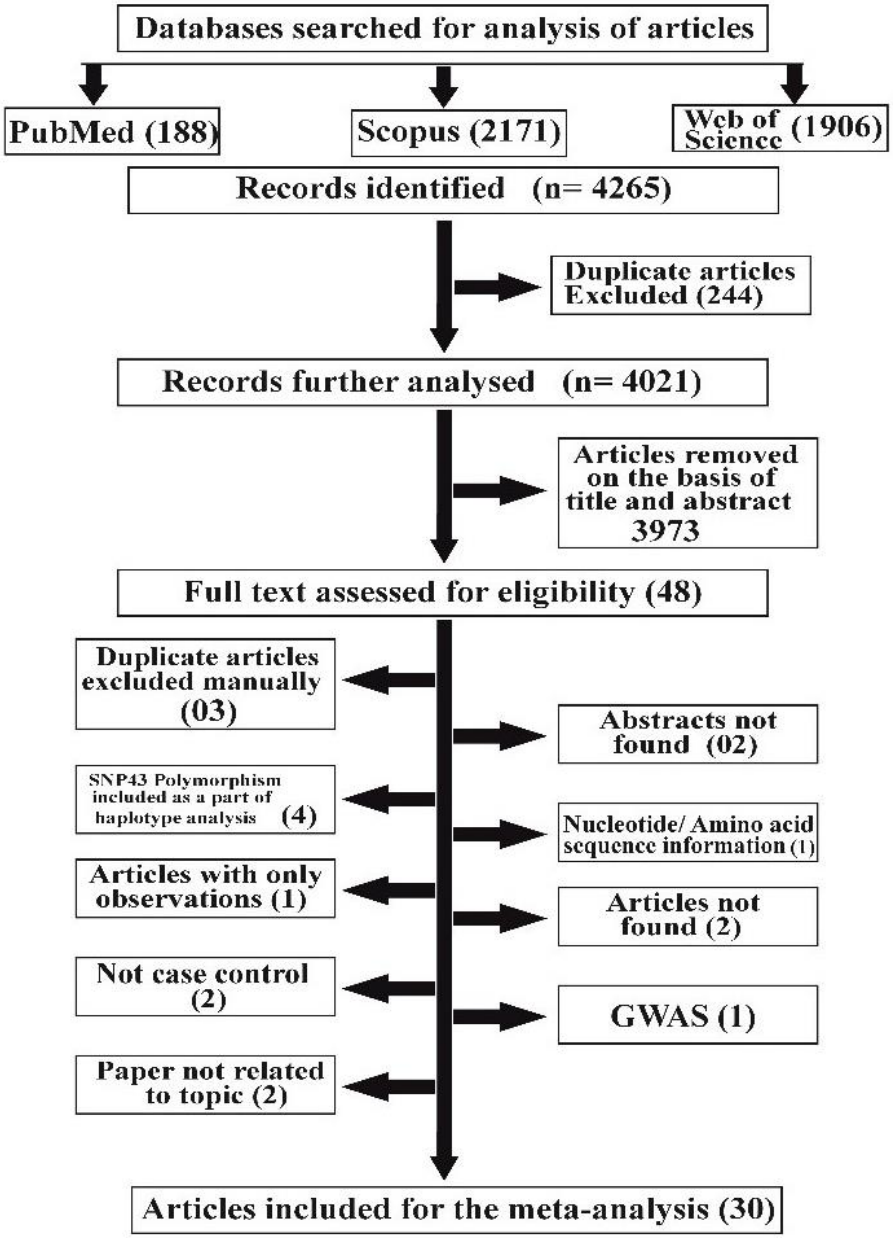

Fig. 1. Flow chart depicting literature search and paper selection process

NOS Scores: Each of the 30 studies included were given a Newcastle–Ottawa Scale (NOS), which ranged from 05-08 (Table 1)

Table 1. Details of the studies included in the meta-analysis

First Author (Publication Year)	Regional Population	Subgroup	Sample size Case/Control	Genotyping method	Quality Score (NOS)
Sultana M (2023) [17]	Bangladeshi	South Asian	202/75	PCR	8
Sarkar P (2020) [18]	Indian	South Asian	104/176	PCR	7
Osman H (2019) [19]	Alexandria University	Other (Alexandria University)	100/50	PCR	6
Bayramcı NS (2017) [20]	Turkish	Middle Eastern	115/100	PCR-RFLP	7
Picos-Cárdenas VJ (2015) [21]	Mexican mestizos	Mexican and Hispanic	211/152	Real time PCR	5
Mendez YL (2015) [22]	Ciudad Juárez, Mexico	Mexican and Hispanic	43/64	PCR	7
Arslan E (2014) [23]	Turkish	Middle Eastern	118/93	PCR-RFLP	6
Buraczynska M (2013) [24]	Caucasians of polish origin	European	880/560	PCR	6
Sharma R (2013) [25]	Indian	South Asian	550/548	PCR	7
Danquah I (2013) [26]	Ghana	African Descent	674/374	PCR	7
Plengvidhya N (2012) [27]	Thai	South Asian	305/250	Multiplex PCR & DHPLC	6
Bodhini D (2011) [28]	Indian	South Asian	649/794	PCR	6
Zaharna MM (2010) [29]	Gaza	Middle Eastern	48/48	PCR-RFLP	5
Ezzidi I (2010) [30]	Tunisian	African Descent	917/748	PCR-RFLP	8
Ezzidi I (2010) [31]	Tunisian	African Descent	917/748	PCR-RFLP	7
Alsaraj F (2010) [32]	Irish	European	227/120	PCR	7
Adak S (2010) [33]	East Indian Population	South Asian	200/100	PCR-RFLP	7
Ouederni TB (2009) [34]	Tunisian	African Descent	140/176	PCR	6
Demirci H (2008) [35]	Turkish	Middle Eastern	165/61	PCR-RFLP	5
Chen SF (2007) [36]	Chinese	East Asian	493/553	PCR-RFLP	7
Kang ES (2006) [37]	Korean	East Asian	454/236	MS-PCR	7
Einarsdottir E (2006) [38]	Sweden	European	777/774	PCR	5
Chen Y (2005) [39]	West African and African American	African Descent	682/268	PCR, Pyrosequencing	5
Wu B (2005) [40]	Chinese	East Asian	168/104	PCR	6
Iwasaki N (2005) [41]	Japanse	East Asian	653/975	Taq Man-based PCR	7
del Bosque-Plata L (2004) [42]	Mexican population	Mexican and Hispanic	132/112	PCR– RFLP	7
Rasmussen SK (2002) [43]	Scandinavian Caucasians	European	409/200	PCR-RFLP	6
Malecki MT (2002) [44]	Polish Population	European	229/148	PCR	7
Fingerlin TE (2002) [45]	Finnish	European	110/112	PCR	5
Tsai HJ (2001) [46]	Samoans	European	172/96	PCR	6

3.2 Sub-Grouping Based on Ethnicity and Genotyping Method

Details like first author's name and year of publication, region where the study was conducted or ethnicity of participants, the number of cases and controls, genotyping method and data on genotypic frequencies of CAPN 10 SNP 19 polymorphism of both cases and controls are mentioned in Table 1.

The 30 papers were sub grouped into South Asian (06), Middle Eastern (04), Mexican and Hispanics (03), European (07), African Descent (05) and East Asians(04) based on ancestry or ethnicity. One study could not be categorized as it involved students of Alexandria University whose ancestry might be varied and were not mentioned in the paper. The genotyping methods included restriction fragment length polymorphism followed by PCR (RFLP-PCR), Taqman assay, mass spectrometry, direct sequencing, real-time PCR etc (Table 1).

3.3 Result of Meta-Analysis

Odds ratio estimates from pooled data involving the 30 studies could not bring to light any significant association of SNP 19 polymorphism with T2DM (Table 2). Fig. 2 depicts the OR estimate of the pooled data under the allele model.

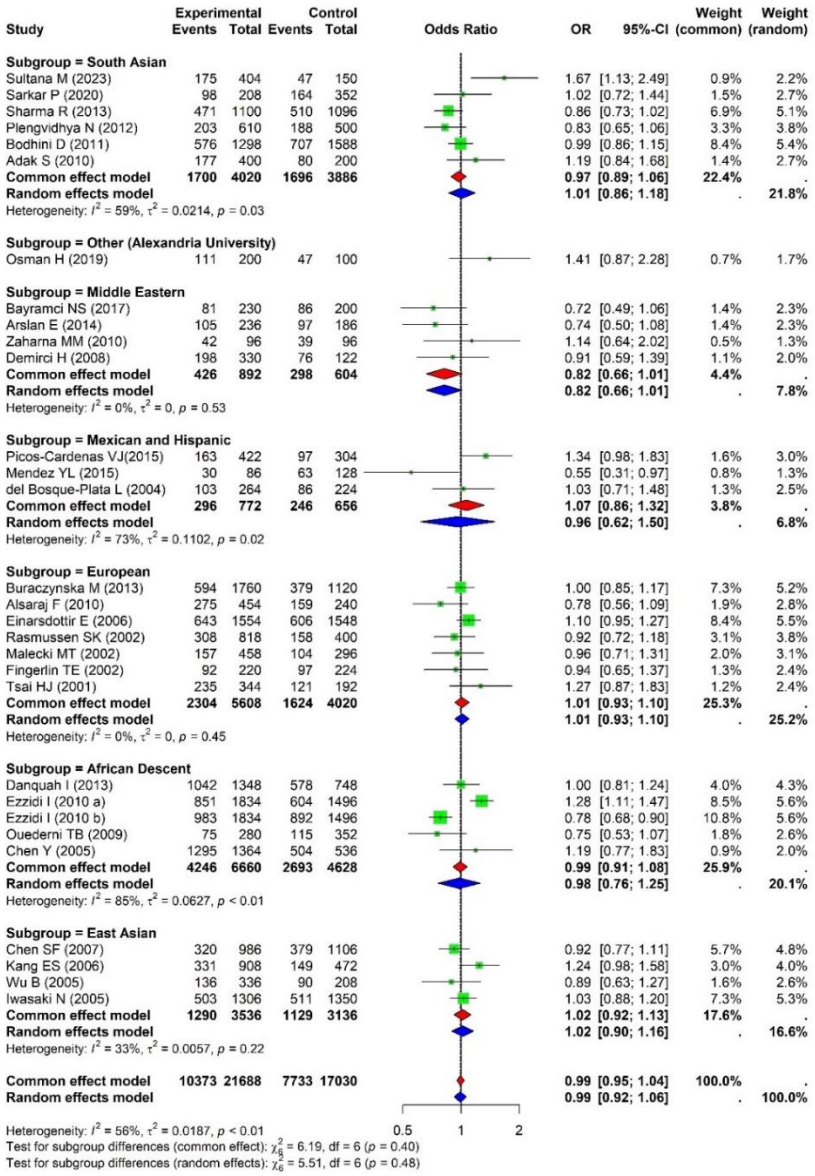

Fig. 2. Forest plot depicting association of CAPN10 SNP 19 polymorphism with T2DM under allele model

The between study heterogeneity was found to be significant in the allele (p<0.01), homozygote (p<0.01), heterozygote (p=0.03) and dominant models (p<0.01) (Table 2). Galbraith plot revealed 4 studies to be the potential outliers (Fig. 3). Removal of these studies removed any significant heterogeneity (Figures not shown). However, it did not affect OR estimates.

3.4 Sub- Group Analysis

Subgroup analysis also did not reveal any significant association of SNP-19 polymorphism with T2DM in any of the seven models considered. Fig. 2 also depicts the subgroup wise OR under the allele model.

3.5 Publication Bias

Visual inspection of asymmetry in Begg's funnel plots derived from each model, indicated some publication bias. Fig. 4 shows funnel plot depicting publication bias under the allele model.

Further, Egger's regression analysis revealed no significant publication bias among the studies (Table 3).

Table 2. Odds Ratio (OR at 95% confidence interval) under different genetic models depicting association of CAPN 10 SNP 19 polymorphism with type 2 diabetes mellitus

Genetic model	No of studies	Number		Test of association OR (95% CI) CEM	Test of association OR (95% CI) REM	Test of heterogeneity	
		Case	Control			I^2 (%)	P_H
Allele model	30	21688	17030	0.99 (0.95; 1.04)	0.99 (0.92; 1.06)	56	<0.01
Homozygote model	30	5867	4568	0.98 (0.89; 1.07)	0.97 (0.84; 1.13)	49	<0.01
Heterozygote model	30	8146	6622	1.02 (0.96; 1.10)	1.02 (0.93; 1.12)	34	0.03
Additive model	30	7675	5860	0.96 (0.89; 1.04)	0.96 (0.89; 1.04)	0	0.48
Dominant model	30	10844	8515	1.01 (0.95; 1.08)	1.01 (0.91; 1.12)	50	<0.01
Recessive model	30	10844	8515	0.97 (0.89; 1.04)	0.97 (0.88; 1.07)	30	0.06
Codominant model	30	10844	8515	1.03 (0.97; 1.09)	1.03 (0.97; 1.09)	0	0.5

REM: Random Effects Model
CEM: Common Effects Model

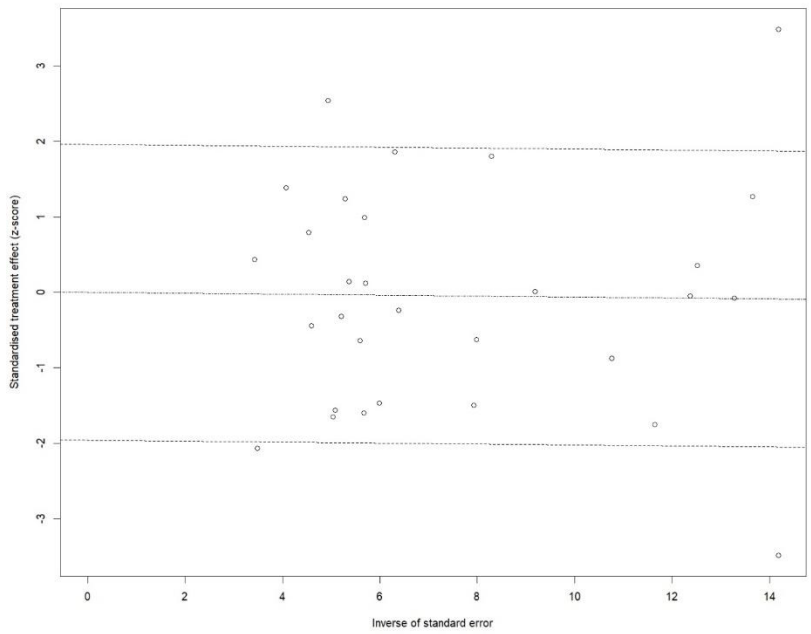

Fig. 3. Galbraith plot depicting potential sources of heterogeneity

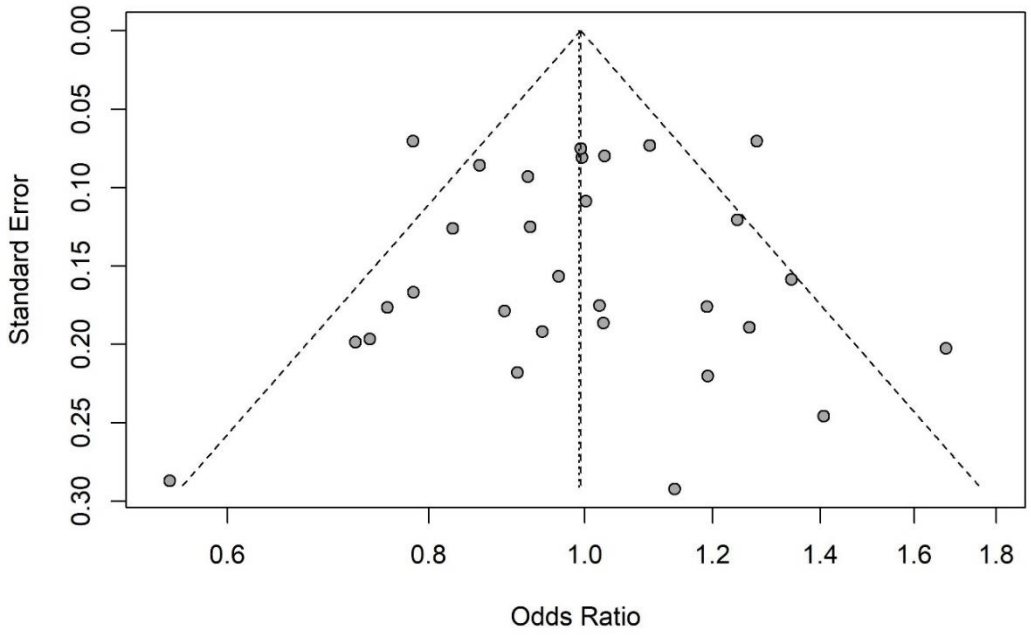

Fig. 4. Funnel plot depicting publication bias under allele model

Table 3. Egger Test values depicting publication bias

Genetic model	No of studies	Number		Test of publication bias
		Case	Control	P Egger
Allele model	30	21688	17030	0.8881
Homozygote model	30	5867	4568	0.9294
Heterozygote model	30	8146	6622	0.9714
Additive model	30	7675	5860	0.9893
Dominant model	30	10844	8515	0.8284
Recessive model	30	10844	8515	0.8744
Codominant model	30	10844	8515	0.9326

4. DISCUSSION

It is very clear from this meta-analysis, that SNP-19 polymorphism of the CAPN-10 gene does not have any effect on the etiology of T2DM. Since, it is an in-del polymorphism,we assumed it to have some effect on CAPN-10 gene expression. However, this robust meta-analysis involving seven different genetic models and taking into account different ethnic groups could not detect any significant association of SNP-19 polymorphism with T2DM under both the common effects and random effects models.

Conversely, various haplotypes and diplotypic combinations involving SNP-19 might have an association with T2DM. Horikawa et al. (2000) [2] were the first to show the combination 112/121 involving polymorphisms at three SNPs namely, SNP-43, SNP-19 and SNP-63 from the CAPN-10 gene to be conferring 2.8, 2.55 and 4.97 folds higher risks of T2DM in the Mexican-Americans, Finnish and Germans respectively. Later, the diplotypic combination 111/112, was found to confer a ten point five folds increased risk of T2DM among the Egyptians [47]. The same combination has also been identified as a culprit in Eastern Indian population by [33]. Amongst the Koreans, the haplotype 122 and diplotype 111/121 were identified as 'at risk' combinations conferring susceptibility to metabolic syndrome [48]. Furthermore, individuals with homozygous haplotype combination of 122/122 have been found to have lower risks of developing metabolic

syndrome compared to other haplotypic combinations in the Egyptians [47]. They also found combinations 111/121 and 122/122 to be conferring protectivity against obesity and thereby development of metabolic syndrome which more often than not leads to diabetes mellitus.

Therefore, while SNP 19 polymorphism alone might have no role to play in the etiology of T2DM, the polymorphism at this locus in combination with other intronic polymorphisms of the CPN 10 gene might play a significant role in either conferring risk or protecting against T2DM.

5. CONCLUSION

This meta-analysis of case control studies involving SNP19 in-del polymorphism of the CAPN10 gene lead to the conclusion that this locus has no role to play in the etiology of type-2 diabetes mellitus. We propose that, while alone the polymorphism at this locus might not be causing any affect on etiology of T2DM, diplotypic and haplotypic combinations of different polymorphisms including the SNP 19 locus might play a role in the etiology of T2DM.

ACKNOWLEDGEMENTS

The authors would like to acknowledge the immense guidance and help provided by colleagues Dr. Shushovan Banik and Dr. Atanu Banerjee, Asst. Professors at the University Department of Zoology, LN Mithila University, Darbhanga, India and Dr. Anupama, Asst. Prof. MRM College Darbhanga during each step of this meta-analysis. Further, help provided during data collection and analysis by Mr. Aman Kumar Jha, Ph. D. research scholar at IIT Kanpur, India and Mr. Suraj Kumar, research scholar at the University Department of Zoology, LN Mithila University is gratefully acknowledged. The authors are also grateful to Prof. A. N. Jha, Head, University Department of Zoology for hugely facilitating the meta-analysis work through provision of high speed internet facility.

The authors would like to acknowledge the helpful comments of two anonymous reviewers who greatly helped in improving the quality of the manuscript.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. GeneCards. GeneCards: The human gene database; 2024.
   Retrieved March 12, 2024
   Available: https://www.genecards.org/cgi-bin/carddisp.pl?gene=CAPN10
2. Horikawa Y, Oda N, Cox NJ, Li X, Orho-Melander M, Hara M, Hinokio Y, Lindner TH, Mashima, H, Schwarz PEH, del Bosque-Plata L, Horikawa Y, Oda Y, Yoshiuchi I, Colilla S, Polonsky KS, Wei S, Concannon P, Iwasaki N, Schulze J, Baier LJ, Bogardus C, Groop L, Boerwinkle E, Hanis CL, and Bell GI. Genetic variation in the gene encoding calpain-10 is associated with type 2 diabetes mellitus. Nat Genet. 2000;26(2): 163–175.
3. Baier LJ, Permana PA, Yang X, Pratley RE, Hanson RL, Shen G-Q, Mott D, Knowler WC, Cox NJ, Horikawa Y, Oda N, Bell GI, Bogardus C. A calpain-10 gene polymorphism is associated with reduced muscle mRNA levels and insulin resistance. Journal of Clinical Investigation. 2000;106(7):R69–R73.
4. Sreenan SK, Zhou Y-P, Otani K, Hansen PA, Currie KPM, Pan C-Y, Lee J-P, Ostrega DM, Pugh W, Horikawa Y, Cox NJ, Hanis CL, Burant CF, Fox AP, Bell GI, Polonsky KS. Calpains Play a Role in Insulin Secretion and Action. Diabetes. 2001;50(9)2013–2020.
5. Goll DE, Thompson VF, LI H, Wei W, Cong J. The Calpain System. Physiol Rev. 2003; 83(3):731–801.
6. Marshall C, Hitman G, Turner M. Calpain-10 regulates insulin secretion. Diabetes. 2003;52:A373.
7. Marshall C, Hitman GA, Partridge CJ, Clark A, Ma H, Shearer TR, Turner MD. Evidence that an Isoform of Calpain-10 Is a Regulator of Exocytosis in Pancreatic β-Cells. Molecular Endocrinology. 2005; 19(1)213–224.
8. Hoffstedt J, Rydén M, Löfgren P, Orho-Melander M, Groop L, Arner P. Polymorphism in the Calpain 10 gene influences glucose metabolism in human fat cells. Diabetologia. 2002;45(2);276–282.
9. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. International Journal of Surgery. 2010;8(5):336–341.

10. Sarhangi N, Sharifi F, Hashemian L, Hassani Doabsari M, Heshmatzad K, Rahbaran M, Jamaldini SH, Aghaei Meybodi HR, Hasanzad M. PPARG (Pro12Ala) genetic variant and risk of T2DM: a systematic review and meta-analysis. Sci Rep. 2020;10(1);12764.
11. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol. 2010;25(9):603–605.
12. Mantel N, Haenszel W. Statistical aspects of the analysis of data from retrospective studies of disease. J Natl Cancer Inst. 1959;22(4):719–48.
13. Higgins JPT. Measuring inconsistency in meta-analyses. BMJ. 2003;327(7414): 557–560.
14. Galbraith RF. A note on graphical presentation of estimated odds ratios from several clinical trials. Stat Med. 1988;7(8); 889–894.
15. Morales J, Welter D, Bowler EH, Cerezo M, Harris LW, McMahon AC, Hall P, Junkins HA, Milano A, Hastings E, Malangone C, Buniello A, Burdett T, Flicek P, Parkinson H, Cunningham, F, Hindorff LA, MacArthur JAL. A standardized framework for representation of ancestry data in genomics studies, with application to the NHGRI-EBI GWAS Catalog. Genome Biol. 2018;19(1):21.
16. Egger M, Smith GD, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ. 1997; 315(7109):629–634.
17. Sultana M, Islam MdM, Hossain Md M, Rahman MdA, Das SC, Barman DN, Mitu FS, Gupta S Das. Association of CAPN10 gene (rs3842570) polymorphism with the type 2 diabetes mellitus among the population of Noakhali region in Bangladesh: A case-control study. Genomics Inform. 2023;21(3):e33.
18. Sarkar P, Chatterjee D, Bandyopadhyay AR. Association of CAPN10 (SNP-19) genetic polymorphism and obesity with T2DM: a study on Bengali Hindu caste population. Int J Diabetes Dev Ctries. 2021;41(1):37–42.
19. Osman H, Osman M, Alsaidy A. GSTT1, Calpain 10 SNP 19 and indices of glycaemia in type 2 diabetes. Br J Biomed Sci. 2019;76(4);205–207.
20. Bayramci NS, Acik L, Kalkan Ç, Yetkin İ. Investigation of glucocorticoid receptor and calpain-10 gene polymorphisms in Turkish patients with type 2 diabetes mellitus. Turk J Med Sci. 2017;47:1568–1575.
21. Picos-Cárdenas VJ, Sáinz-González E, Miliar-García A, Romero-Zazueta A, Quintero-Osuna R, Leal-Ugarte E, Peralta-Leal V, Meza-Espinoza JP. Calpain-10 gene polymorphisms and risk of type 2 diabetes mellitus in Mexican mestizos. Genet Mol Res. 2015;14(1): 2205–2215.
22. Loya Méndez Y, Reyes Leal G, Sánchez González A, Portillo Reyes V, Reyes Ruvalcaba D, and Bojórquez Rangel G. [SNP-19 genotypic variants of CAPN10 gene and its relation to diabetes mellitus type 2 in a population of Ciudad Juarez, Mexico]. Nutr Hosp. 2014;31(2):744–50.
23. Arslan E, Acik L, Gunaltili G, Ayvaz G, Altinova AE, Arslan M. The effect of calpain-10 gene polymorphism on the development of type 2 diabetes mellitus in a Turkish population. Endokrynol Pol. 2014;65(2):90–5.
24. Buraczynska M, Wacinski P, Stec A, Kuczmaszewska A. Calpain-10 gene polymorphisms in type 2 diabetes and its micro- and macrovascular complications. J Diabetes Complications. 2013;27(1):54–58.
25. Sharma R, Matharoo K, Kapoor R, Chopra H. Bhanwer A. Ethnic differences in CAPN10 SNP-19 in type 2 diabetes: a North-West Indian case control study and evidence from meta-analysis. Genet Res (Camb). 2013;95(5):146–155.
26. Danquah I, Othmer T, Frank LK, Bedu-Addo G, Schulze MB, Mockenhaupt FP. The TCF7L2 rs7903146 (T) allele is associated with type 2 diabetes in urban Ghana: a hospital-based case-control study. BMC Med Genet. 2013;14;96.
27. Plengvidhya N, Chanprasert K, Tangjittipokin W, Thongnoppakhun W, Yenchitsomanus P. Detection of CAPN10 copy number variation in Thai patients with type 2 diabetes by denaturing high performance liquid chromatography and real-time quantitative polymerase chain reaction. J Diabetes Investig. 2015;6(6): 632–639.
28. Bodhini D, Radha V, Ghosh S, Sanapala KR, Majumder PP, Rao MRS, Mohan V. Association of calpain 10 gene polymorphisms with type 2 diabetes mellitus in Southern Indians. Metabolism. 2011;60(5):681–688.

29. Zaharna MM, Abed AA, Sharif FA. Calpain-10 gene polymorphism in type 2 diabetes mellitus patients in the Gaza Strip. Med Princ Pract. 2010;19(6):457–462.
30. Ezzidi I, Mtiraoui N, Nemr R, Kacem M, Al-Khateeb GM, Mahjoub T, Almawi WY. Variants within the calpain-10 gene and relationships with type 2 diabetes (T2DM) and T2DM-related traits among Tunisian Arabs. Diabetes Metab. 2010;36(5):357–362.
31. Ezzidi I, Turki A, Messaoudi S, Chaieb M, Kacem M, Al-Khateeb GM, Mahjoub T, Almawi WY, and Mtiraoui N. Common polymorphisms of calpain-10 and the risk of Type 2 Diabetes in a Tunisian Arab population: a case-control study. BMC Med Genet. 2010;11:75.
32. Alsaraj F, O'Gorman D, McAteer S, McDermott J, Hawi Z, Sreenan S. Haplotype association of calpain 10 gene variants with type 2 diabetes mellitus in an Irish sample. Ir J Med Sci. 2010;179(2): 269–272.
33. Adak S, Sengupta S, Chowdhury S, Bhattacharyya M. Co-existence of risk and protective haplotypes of Calpain 10 gene to type 2 diabetes in the eastern Indian population. Diab Vasc Dis Res. 2010;7(1): 63–68.
34. Ouederni TB, Sanchez-Corona J, Skhiri HA, Maiz H Ben Abid HK, Benammar-Elgaaied A. Study of association of the SNP19 polymorphism of calpain 10 gene with type 2 diabetes in ethnic sub-groups of the Tunisian population: Gene-environment interaction. Ann Biol Clin (Paris). 2009;67(2):171–176.
35. Demirci H, Yurtcu E, Ergun MA, Yazici AC, Karasu C, Yetkin I. Calpain 10 SNP-44 Gene Polymorphism Affects Susceptibility to Type 2 Diabetes Mellitus and Diabetic-Related Conditions. Genet Test. 2008; 12(2):305–309.
36. Chen S, Lu X, Yan W-L, Huang J, Gu D. Variations in the calpain-10 gene are associated with the risk of type 2 diabetes and hypertension in northern Han Chinese population. Chin Med J (Engl). 2007; 120(24):2218–2223.
37. Kang ES, Kim HJ, Nam M, Nam CM, Ahn CW, Cha BS, Lee HC. A novel 111/121 diplotype in the Calpain-10 gene is associated with type 2 diabetes. J Hum Genet. 2006;51(7):629–633.
38. Einarsdottir E, Mayans S, RuikkaK., Escher SA, Lindgren P, Agren A, Eliasson M, Holmberg D. Linkage but not association of calpain-10 to type 2 diabetes replicated in northern Sweden. Diabetes. 2006;55(6):1879–1883.
39. Chen Y, Kittles R, Zhou J. Chen G, Adeyemo A, Panguluri RK, Chen W, Amoah A, Opoku V, Acheampong J, Agyenim-Boateng K, Eghan BA, Nyantaki A, Oli J, Okafor G, Ofoegbu E, Osotimehin B. Abbiyesuku F, Johnson T, Fasanmade O, Rufus T, Furbert-Harris P, Daniel HI, Berg KA, Collins FS, Dunston GM, Rotimi CN. Calpain-10 gene polymorphisms and type 2 diabetes in West Africans: the Africa America Diabetes Mellitus (AADM) Study. Ann Epidemiol. 2005;15(2):153–159.
40. Wu B, Takahashi J, Fu M, Cheng H, Matsumura S, Taniguchi H. Variants of calpain-10 gene and its association with type 2 diabetes mellitus in a Chinese population. Diabetes Res Clin Pract. 2005; 68(2):155–161.
41. Iwasaki N, Horikawa Y, Tsuchiya T, Kitamura Y, Nakamura T, Tanizawa Y, Oka Y, Hara K, Kadowaki T, Awata T, Honda M, Yamashita K, Oda N, Yu L, Yamada N, Ogata M, Kamatani, N, Iwamoto Y, Bosque-Plata L Del Hayes MG, Cox NJ, Bell GI. Genetic variants in the calpain-10 gene and the development of type 2 diabetes in the Japanese population. J Hum Genet. 2005;50(2):92–98.
42. del Bosque-Plata L, Aguilar-Salinas CA, Tusié-Luna MT, Ramírez-Jiménez S, Rodríguez-Torres M, Aurón-Gómez M, Ramírez E, Velasco-Pérez ML, Ramírez-Silva A, Gómez-Pérez F, Hanis CL, Tsuchiya T. Yoshiuchi I, Cox NJ, Bell GI. Association of the calpain-10 gene with type 2 diabetes mellitus in a Mexican population. Mol Genet Metab. 2004;81(2): 122–126.
43. Rasmussen SK, Urhammer SA, Berglund L, Jensen JN, Hansen L, Echwald SM, Borch-Johnsen K, Horikawa Y, Mashima H, Lithell H, Cox NJ, Hansen T, Bell GI, Pedersen O. Variants within the calpain-10 gene on chromosome 2q37 (NIDDM1) and relationships to type 2 diabetes, insulin resistance, and impaired acute insulin secretion among Scandinavian Caucasians. Diabetes. 2002;51(12):3561–3567.

44. Malecki MT, Moczulski DK, Klupa T, Wanic K, Cyganek K, Frey J, Sieradzki J. Homozygous combination of calpain 10 gene haplotypes is associated with type 2 diabetes mellitus in a Polish population. Eur J Endocrinol. 2002;146(5):695–699.
45. Fingerlin TE, Erdos MR, Watanabe RM, Wiles KR, Stringham HM, Mohlke KL, Silander K, Valle TT, Buchanan TA, Tuomilehto J, Bergman RN, Boehnke M, Collins FS. Variation in three single nucleotide polymorphisms in the calpain-10 gene not associated with type 2 diabetes in a large Finnish cohort. Diabetes. 2002;51(5):1644–1648.
46. Tsai HJ, Sun G, Weeks DE, Kaushal R, Wolujewicz M, McGarvey ST, Tufa J, Viali S, Deka R. Type 2 diabetes and three calpain-10 gene polymorphisms in Samoans: no evidence of association. Am J Hum Genet. 2001;69(6):1236–1244.
47. El-Far SW, Kassem HSh, Embaby AM, Saad AA, Mowafy N, Haroun M. Association of CAPN10 haplotype combinations with type 2 diabetes mellitus and metabolic syndrome among Egyptians: pilot study—genotyping of three CAPN10 variants. Egyptian Journal of Medical Human Genetics. 2022;23(1):26.
48. Shima Y, Nakanishi K, Odawara M, Kobayashi T, Ohta H. Association of the SNP-19 genotype 22 in the calpain-10 gene with elevated body mass index and hemoglobin A1c levels in Japanese. Clinica Chimica Acta. 2003;336(1–2):89–96.

Peer-review history:
The peer review history for this paper can be accessed here:
https://prh.mbimph.com/review-history/3404