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MSc Program: Methodology of Biomedical Research, Biostatistics and Clinical Bioinformatics

Msc Final Paper

Assess the reporting quality of case-controlled trials of the variant TNF in diabetic nephropathy, based on STROBE statement

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Preface

At this point, before embarking on presenting the paper, I would like to take a moment to reflect on the 2014-2015 academic year. It has certainly been a difficult year. Work, studies, and family life, all bundled up in one beautiful mess. Yet, it all went well, everything worked out for the best and I know that I came out a better person. Nonetheless I feel I would not have done it, had it not been for the invaluable help I received from some very important people in my life.

Firstly, I wish to thank the honorable Professor Elias Zintzaras, both for his assistance during this academic year and for introducing me to the world of clinical trials, which led me to fall in love with this field.

It is also for the same reasons that I wish to thank my supervisor Professor Dr Ioannis Stefanidis, not forgetting his help in structuring and writing this paper.

I also wish to thank my husband, Mr. Andreas Sophiadis, as well as my parents, for their support and patience during this year.

Over this past year I met several great people, with many of whom I formed strong bonds of friendship, through mutual support, help, and solidarity. Therefore, many thanks go to my friends and colleagues Eugenia Karakou and Maria Strataki for all the time we spent together, supporting each other and trying to find solutions to problems we were faced with.

Thank you!

1. Introduction

1.1 What are clinical research/trials?

Clinical research has been defined to cover different scopes. Some of the definitions are given below.

The US national institutes of health define clinical research as a patient-oriented conducted research system, where either human beings are the subjects or materials are subjected to study (Richesson and Andrews, 2012). So the broad areas that are covered under this definition include therapeutic investigation, human diseases development mechanisms, up-comings of new technology, behavioural studies, epidemiology and even health services.

Clinical research may refer to drug bibliography. In other words, it involves the development of tested articles in the laboratory to the point at which it reaches the intended user (consumers in the market. Once a molecule has been identified in the laboratory, its aspects are explored by subjecting it to study (Nichd.nih.gov, 2015).

Usually, clinical research is carried out at academic centres of medical. These centres offer Prestige of the academic institution and give access to metropolitan. This has availed a pool of volunteers as well as medical participants. (Keck.usc.edu, 2015).

1.2 What are case-controlled clinical trials?

Clinical trials are key in an assessment of the medicine safety and their effectiveness (RAVINA, B. 2012). The major drawback of a clinical trial is that the population sample use for the trial may not be a true representation of the entire population. Therefore, inaccurate conclusions may be made.

Case-control is one of the types of observational studies. It involves using the cases (those with the outcome of the interest) and controls (those without the outcome of interest). The criteria for selecting these categories of the groups should be known and made clear. After the selection, the exposure is administered in the two groups, and the correct observation is made. One of the major advantages of the method is that it is cheap and is very useful in conducting research on rare diseases. The study has an objective of relating the exposure and the outcome.

According to Porta's Dictionary of Epidemiology, case-control study is described as observational epidemiology in which persons of interest (outcome variable) are studied alongside control group (reference group) (Younger, 2009).

A case-control study is preferred when the disease being studied is rare. In such a case-cohort study is impractical (ROTHMAN, 2008, p.112).

1.3 What is the TNF variant in diabetic nephropathy?

1.3.1 Entrez Gene summary for TNF Gene

This gene handles encoding pointflammatory cytokine that performs multifunction. It performs its operations through the receptors TNNFRSF1B/TNFBR and TNFRSF1A/TNFR1. This cytokine regulates some biological processes. Some of the biologically regulated processes include lipid metabolism, apoptosis differentiation and coagulation. Cytokine is implicated in various diseases even in autoimmune diseases, cancer and insulin. In mice, knockout studies, have given a suggestion that cytokine has a neuro-protective function. [Provided by RefSeq, Jul 2008].

Figure 1.1 shows a cytogenetic band.

Figure 1. 1 cytogenetic band (Database, 2015).

1.3.2 GeneCards Summary for TNF Gene

TNF is protein in nature, and it is a coding gene. Some of the diseases associated with TNF are aphthous stomatitis and mycobacterium chelonae. Some of its pathways are Proteoglycans in cancer and MARK signalling pathway (Database, 2015). The gene is related to GO annotations that include cytokine activity and identical protein binding. The gene important Para log is TNFSF15.

1.3.3 UniProtKB/Swiss-Prot for TNF Gene TNFA_HUMAN,P01375

This is a cytokine that binds to TNFRSF1B/TNFBR and TNFRSF1A/TNFR1. It causes fever in either through direct action or stimulation (interleukin-1 secretion is stimulated). In certain conditions, cell proliferation is stimulated, and this leads to induction of cell differentiation. Treg (impairs regulatory T-cells) do function in persons having rheumatoid arthritis through FOXP3 dephosphorylation. Treg cells are rendered functionally defective if FOXP3 are inactivated (Database, 2015).

1.3.4 What is STROBE?

Most researches in the medical field are observational in nature (MAGNUS, M. 2009). Therefore, reporting may be of low quality for this reason STROBE statement was developed to carb the problem. The term STROBE stands for strengthening the Reporting of Observational Studies in Epidemiology. STROBE Statement is, therefore, a guideline consisting of twenty-two items that are considered to render good reporting in observational studies. Its publications have been done in most biomedical journals for the obvious reasons. Its founder is International Committee of Medical Journal Editors (Strobe-statement.org, 2015).

Case-control study, cohort study and cross-sectional study do share eighteen items of the STOBE Statement. Four items are specific to each type of the observational study. Its main objective is to improve reporting quality (Strobe-statement.org, 2015).

Table 1.1 shows the TROBE statement entailing all the items used in strengthening the quality of the report concerning epidemiology.

STROBE Statement—which is a Checklist of items that are included in reports of case-control *Studies*

	Item No	**Recommendation**
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found

Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any pre-specified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls
		(*b*) For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, explain how matching of cases and controls was addressed
		(*e*) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—e.g. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram

Descriptive data	14*	(a) Give characteristics of study participants (e.g. demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
Outcome data	15*	Report numbers in each exposure category, or summary measures of exposure
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—e.g. analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalizability	21	Discuss the generalizability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

Table 1. 1 : (STROBE statement: guidelines for reporting observational studies, 2007)

2. Objective

The objective of this paper is to evaluate/assess, using the STROBE statement checklist, the reporting quality of case-controlled trials of the variant TNF in diabetic nephropathy.

In essence, the researcher will compile a list of case-controlled trial papers and mark, or grade them, according to the checklist provided Table 1.1. Each paper will be examined and the researcher will look for the points mentioned in the STROBE statement checklist. It goes without saying that the more points a paper satisfies, the more reliable it can be deemed in the eyes of the medical community, as it follows a predetermined set of rules and satisfies a series of conditions that make it more medically useful.

3. Methodology

This analysis is based on a sample of eight reports of case-controlled trials. The case-controlled study is based on the topic variant tumour necrosis factor (TNF) in diabetic nephropathy. Eight relevant journal articles for the study were obtained online. The articles were picked based on relevancy. Relevancy was checked based on the research topic of the article. The articles picked were analysed by employing the principles of a case-controlled study; one of the methods of the observational study.

The STROBE Statement is used as the assessment tool. Each and every article is read and then cross-checked with the STROBE Statement (checklist). The process of crosschecking is done per subtopic as provided by the STROBE Statement. For example, an introduction section of the article is read and verified whether it has a scientific background and the rationale of undertaking such a study.

Marks are awarded to each point stated in the section if that point is a requirement of the STROBE Statement. The distribution of marks is as follows: one mark for every point fulfilled, half a mark is awarded for every partially fulfilled point and finally zero for non-fulfilled point. The grand score is reached by summing all the marks scored. Percentage calculation is done by the formula shown below:

$$\%score = \frac{x}{22} \times 100 \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots$$

Where x is the marks awarded to the article. 22 is the total marks that can be attained if all the STROBE Statement points are adhered to.

The process is repeated for the eight articles. The scores obtained are then grouped together according to the scores. The number of groups required are four, broken down

into 4 tiers, based on score percentage. These tiers are 0.00-24.99%, 25.00-49.99%, 50.00-74.99% and 75.00-100%. All percentages are calculated using the aforementioned formula, by inputting the score obtained after assessing each article using the STROBE statement.

Once the grouping is done the process of analysis commences. If the percentage scored by the majority of articles is high, then the STROBE statement has high quality for case-controlled study. On the other hand, if the marks scored by the majority of articles is low, then the quality of the STROBE statement may be considered to be low.

4. Results

The seven articles have been analysed as stated in the methodology. Tables are used to ease the analysis. Explanations are provided within the tables. Each article has its own table. The name of the article is used as the name of the table.

4.1 Genetics of diabetic nephropathy (Lee et al., 2005).

	Item No	Item	Remarks	Score
Title and abstract	1	Title and abstract	The term diabetic nephropathy, which appears in the title, is the study's design.	1
			Task performed and results found are described in the abstract. Hence the abstract is a balanced summary and informative.	
Introduction	2	Background	Scientific definition of diabetic nephropathy is given and other additional scientific information is provided. So scientific background is fully satisfied. The rationale of the study is provided.	1
	3	Objectives	The study aims at providing conclusive results on the research subjects (Lee et al., 2005). Therefore, clarity in specific objectives.	1
Methods	4	Study design	Key elements are availed early and they are as follows: TNF-alpha -308G/A Polymorphism Gene	1

			Diabetic nephropathy Meta-analysis	
	5	Setting	Location-provided e.g. Cochrane Library. Relevant dates-provided e.g. March 10, 2013- last search date.	1
	6	Participants	Selection criteria availed and the rationale for following such criteria.	1
			Matched studies-not applicable for this case.	
	7	Variables	Outcomes and predictors are clearly defined.	1
	8	Data sources & measurements	Well stated.	1
	9	Bias	Analyzed through visual inspection	1
	10	Study size	Study size is stated.	1
	11	Quantitative variables	Very clear.	1
	12	Statistical methods	All statistical methods are adhered to e.g. use of z-test, analysis of sensitivity among others.	1
Results	13	Participant	At every stage the study size is provided. Reasons for disqualification are given Flow diagram is used in showing the study size at every stage and providing reasons for the disqualification.	1
	14	Descriptive data	Clinical participant Missing data not stated.	1
	15	Outcome data	Outcome data-provided.	1
	16	Main results	Precision of 95% CI is used; relative risk to absolute risk -not applicable for this case; category boundaries-not applicable for this case.	1
	17	Other analysis	Both subgroups and sensitivity are analyzed	1
Discussion	18	Key results	Results are given in line with the objectives.	1
	19	Limitations	Stated e.g. only two ethnic groups were used so it may only be applicable to those groups (Lee et al., 2005).	1
	20	Interpretation	Provided as per the requirement.	1
	21	Generalizability	External validity-provided.	1
Other	22	Source of	Not mentioned.	0

information		funding and their role		
	Grand score			**21**

Table 4. 1 Article of Genetics of diabetic nephropathy (Lee et al., 2005)

4.2 Journal of Diabetes and Its Complications (Gupta et al., 2015).

	Item No.	Item	Remarks	Score
Title and abstract	1	Title and abstract	The term diabetes, which appears in the title, is the study's design. Task performed and results found are described in the abstract. The abstract constitutes a balanced and informative summary.	1
Introduction	2	Background	Chronic kidney disease is described as a world health problem (Gupta et al., 2015); and more information and scientific background is provided.	1
	3	Objectives	Polymorphisms might play a crucial role in the pathogenesis and development of DN (Gupta et al., 2015). The above hypothesis is provided.	1
Methods	4	Study design	Absence of key elements early in the paper.	0
	5	Setting	Locations indicated e.g. Bahadur Hospital Relevant dates: starting time of study provided as October 2010 and completion time provided as April 2012 (Gupta et al., 2015).	1
	6	Participants	Selection criteria availed e.g. group II: patients with T2DM for greater or equal 10 years without nephropathy (DM) (Gupta et al., 2015). Matched studies-not applicable.	1
	7	Variables	Outcomes and predictors are clearly defined.	1
	8	Data sources & measurements	Clearly stated.	1
	9	Bias	Not analyzed.	0
	10	Study size	Study size of 300 subjects used.	1
	11	Quantitative variables	Very clear. Three groupings were made.	1
	12	Statistical methods	All statistical methods are adhered to e.g. use of t-test.	1
Results	13	Participant	Study size is provided at the beginning of the study.	0.5
	14	Descriptive data	Both demographic (since sex and age are included) and clinical participant Missing data not mentioned.	0.5

	15	Outcome data	Outcome data-provided.	1
	16	Main results	Unadjusted estimates and adjusted estimates are provided.	1
	17	Other analysis	No analysis of subgroups and sensitivity.	0
Discussion	18	Key results	Not clear.	0.5
	19	Limitations	Stated large sample is required to justify the feasibility of the polymorphisms (Gupta et al., 2015).	1
	20	Interpretation	Provided.	1
	21	Generalizability	External validity-provided.	1
Other information	22	Source of funding and their role	Indian Council of Medical Research and University College of Medical Sciences, New Delhi (Gupta et al., 2015). They supported the research partially.	1
	Grand score			**18.5**

Table 4. 2 Journal of diabetes and its complications (Gupta et al., 2015)

4.3 Association of of TGFβ1, TNFα, CCR2 and CCR5 gene polymorphisms (Prasad et al., 2007).

	Item No.	Item	Remarks	Score
Title and abstract	1	Title and abstract	The term Association, which appears in the title, is the study's design. Task performed and results found are described in the abstract. The abstract constitutes a balanced and informative summary.	1
Introduction	2	Background	Diabetes type 2 is described in the background; more is provided and so is scientific background.	1
	3	Objectives	Association of TGFβ1, TNFα, CCR2 and CCR5 gene polymorphisms in type-2 diabetes and renal insufficiency among Asian Indians (Prasad et al., 2007). The above objective is provided.	1
Methods	4	Study design	Key elements: Cytokines Diabetes mellitus Diabetic nephropathy Inflammation Mononuclear cells Are provided early in the paper of concern.	1
	5	Setting	Locations clear. Relevant dates mentioned.	1
	6	Participants	Selection criteria availed. Matched studies-not applicable.	1
	7	Variables	Outcomes and predictors are clearly defined.	1
	8	Data sources & measurements	Clearly stated.	1
	9	Bias	Not analyzed.	0
	10	Study size	Study size not clear, though implied through mention of trial sites (Prasad et al., 2007).	1
	11	Quantitative variables	Clear.	1
	12	Statistical methods	Statistical methods are adhered to e.g. use of t-test.	1

Results	13	Participant	Study size is not provided clearly at every stage of the study.	0.5
	14	Descriptive data	Demographic data provided in the background in the paper. Missing data not mentioned.	0.5
	15	Outcome data	Outcome data-provided.	1
	16	Main results	Unadjusted estimates and adjusted estimates are provided.	1
	17	Other analysis	There is analysis of sensitivity.	1
Discussion	18	Key results	Not clear.	0.5
	19	Limitations	Limited to population that provided the sample.	1
	20	Interpretation	Provided.	1
	21	Generalizability	Outcome not clearly generalized, because it is not mentioned whether the results obtained would extend to other population outside the population sample.	0.5
Other information	22	Source of funding and their role	Not mentioned.	0
	Grand score			**18.0**

Table 4. 3 Association of of TGFβ1, TNFα, CCR2 and CCR5 gene polymorphisms (Prasad et al., 2007)

4.4 Association between LTA, TNF and AGER Polymorphisms and Late Diabetic Complications (Lindholm et al., 2008).

	Item No.	Item	Remarks	Score
Title and abstract	1	Title and abstract	The terms Association and polymorphisms, which appear in the title, is the study's design. Activities performed and results found are described in the abstract. Hence the abstract is balanced and informative summary.	1
Introduction	2	Background	Has scientific background due to description of scientific terms like polymorphisms and complications, among others.	1
	3	Objectives	The aim of this study is to seek an association between LTA, TNF and AGER Polymorphisms and Late Diabetic Complications, through analysis of results.(Lindholm et al., 2008).	1
Methods	4	Study design	Key elements: Association LTA TNF AGER polymorphisms Provided early in the paper of concern.	1
	5	Setting	Locations not provided. Relevant dates not mentioned.	0
	6	Participants	Selection criteria made available.	1
	7	Variables	Outcomes and predictors are clearly defined.	1
	8	Data sources & measurements	Clearly stated.	1
	9	Bias	Mentioned but not analyzed.	0.5
	10	Study size	Study size mentioned.	1
	11	Quantitative variables	Clear.	1
	12	Statistical methods	Statistical methods are adhered to e.g. use of t-test.	1
Results	13	Participant	Study size is provided at every stage of the study.	1
	14	Descriptive data	Demographic and clinical	0.5

			Missing data not mentioned.	
	15	Outcome data	Outcome data-provided.	1
	16	Main results	Unadjusted estimates and adjusted estimates are provided.	1
	17	Other analysis	Sensitivity is analyzed.	1
Discussion	18	Key results	Clear.	1
	19	Limitations	Small sample of type 1 diabetic patients, which could lead to misrepresentation (Lindholm et al., 2008).	1
	20	Interpretation	Provided.	1
	21	Generalizability	Made clearly.	
Other information	22	Source of funding and their role	Mentioned in the acknowledgements of the assessed paper.	1
	Grand score			**19.0**

Table 4. 4 Association between LTA, TNF and AGER Polymorphisms and Late Diabetic Complications (Lindholm et al., 2008)

4.5 Association of interleukin-10 polymorphisms with cytokines in type 2 diabetic nephropathy. (Kung et al., 2010).

	Item No.	Item	Remarks	Score
Title and abstract	1	Title and abstract	The terms association and polymorphisms, which appear in the title, is the study's design. Abstract provides activities performed and results obtained hence it is very informative and balanced.	1
Introduction	2	Background	Description of scientific terms like interleukin-10 polymorphism is made (Kung et al., 2010). Hence, scientific background.	1
	3	Objectives	Aim of this study is to seek an association of interleukin-10 polymorphisms with cytokines in type 2 diabetic nephropathy (Kung et al., 2010).	1
Methods	4	Study design	Key elements were presented earlier in the paper.	1
	5	Setting	The setting is menioned (Taiwan) Relevant dates are also mentioned.	1
	6	Participants	Selection criteria availed-selection from patient pool (Kung et al., 2010).	1
	7	Variables	Outcomes and predictors are clearly defined.	1
	8	Data sources & measurements	Clearly stated.	1
	9	Bias	Analysed.	1
	10	Study size	Study size is clearly stated (Kung et al., 2010).	1
	11	Quantitative variables	Clear.	1
	12	Statistical methods	Statistical methods are adhered to e.g. use of logistic regression analysis (Gruden et al., 2012).	1
Results	13	Participant	Study size is provided at every stage of the study.	1
	14	Descriptive data	Demographic and clinical Missing data not mentioned.	0.5
	15	Outcome data	Outcome data-provided.	1
	16	Main results	Unadjusted estimates and adjusted estimates are provided.	1
	17	Other analysis	Sensitivity is analysed.	1
Discussion	18	Key results	Not clear.	0.5

	19	Limitations	Miscalculation of case subjects and controls could have led to errors (Kung et al., 2010).	1
	20	Interpretation	Provided.	1
	21	Generalizability	Made clear.	1
Other information	22	Source of funding and their role	Not mentioned.	0
	Grand score			**20.0**

Table 4. 5 Article on the Association of interleukin-10 polymorphisms with cytokines in type 2 diabetic nephropathy. (Kung et al., 2010)

4.6 Gene (Dabhi and Mistry, 2015)

	Item No.	Item	Remarks	Score
Title and abstract	1	Title and abstract	The term gene, which appears in the title, is the study's design. Abstract provides activities performed and results obtained hence it is very informative and balanced.	1
Introduction	2	Background	Description of scientific terms like diabetic nephropathy is made; and more other scientific description. Hence, scientific background.	1
	3	Objectives	The aim of this study is to understand the role of cytokine gene polymorphism and oxidative stress on pathophysiology of diabetes and on the onset of secondary complications (Dabhi and Mistry, 2015).	1
Methods	4	Study design	Key elements: TNF-α gene polymorphism IL-1α gene polymorphism Diabetes Diabetic nephropathy Oxidative stress West Indian population Presented earlier in the paper.	1
	5	Setting	Locations West Indian Relevant dates not mentioned.	0.5
	6	Participants	Selection criteria availed.	1
	7	Variables	Outcomes and predictors are clearly defined.	1
	8	Data sources & measurements	Clearly stated.	1
	9	Bias	Not analysed.	0
	10	Study size	Study size provided with a control group of 235.	1
	11	Quantitative variables	Clear.	1
	12	Statistical methods	Statistical methods are adhered to e.g. use of chi-test.	1
Results	13	Participant	Study size is provided.	0.5
	14	Descriptive data	Demographic and clinical (evidenced by table 1)	0.5

			Missing data not mentioned.	
	15	Outcome data	Outcome data-provided.	1
	16	Main results	Unadjusted estimates and adjusted estimates are provided.	1
	17	Other analysis	Sensitivity is not analysed.	0
Discussion	18	Key results	Not clear.	0.5
	19	Limitations	Not clear.	0.5
	20	Interpretation	Provided.	1
	21	Generalizability	Made clearly.	1
Other information	22	Source of funding and their role	Mentioned e.g Charutar Vidya Mandal (Dabhi and Mistry, 2015).	1
	Grand score			**17.0**

Table 4. 6 Article of Gene (Dabhi and Mistry, 2015)

4.7 Genetic Determination of TNF and Myeloperoxidase Production in Dialyzed Patients with Diabetic Nephropathy (Buraczynska et al., 2004).

	Item No.	Item	Remarks	Score
Title and abstract	1	Title and abstract	The term genetic determination, which appears in the title, is the study's design. Abstract provides activities performed and results obtained are very informative and balanced.	1
Introduction	2	Background	Description of scientific terms like Myeloperoxidase Production, are made clear in the introduction; and further scientific description. Hence, scientific background.	1
	3	Objectives	The aim of this study is to determine the genetic makeup of TNF and Myeloperoxidase Production in Dialyzed Patients with Diabetic Nephropathy (Buraczynska et al., 2004).	1
Methods	4	Study design	Key elements presented earlier in the paper.	1
	5	Setting	Locations: Hospital of the researchers Relevant dates mentioned in the paper (Buraczynska et al., 2004).	1
	6	Participants	Selection criteria availed.	1
	7	Variables	Outcomes and predictors are clearly defined.	1
	8	Data sources & measurements	Clearly stated.	1
	9	Bias	Not analysed.	0
	10	Study size	Study size provided.	1
	11	Quantitative variables	Clear.	1
	12	Statistical methods	Statistical methods are adhered.	1
Results	13	Participant	Study size is provided.	1
	14	Descriptive data	Demographic and clinical Missing data not mentioned.	0.5
	15	Outcome data	Outcome data-provided.	1
	16	Main results	Unadjusted estimates and adjusted estimates are provided.	1

	17	Other analysis	Sensitivity is partially analysed.	0.5
Discussion	18	Key results	Made clear.	1
	19	Limitations	Made clear.	1
	20	Interpretation	Provided.	1
	21	Generalizability	Made clear.	1
Other information	22	Source of funding and their role	Mentioned in the acknowledgement	1
	Total score			**20.0**

Table 4. 7 Genetic Determination of TNF and Myeloperoxidase Production in Dialyzed Patients with Diabetic Nephropathy (Buraczynska et al., 2004).

4.8 Predictive value of cytokine gene polymorphisms for the development of end-stage renal disease (Babel et al., 2006).

	Item No.	Item	Remarks	Score
Title and abstract	1	Title and abstract	The term predictive value, which appears in the title, is the study's design. Abstract provides activities performed and results obtained are very informative and balanced.	1
Introduction	2	Background	Description of scientific terms like cytokine gene polymorphisms, are made clear in the introduction; and further scientific description. Hence, scientific background.	1
	3	Objectives	The aim of this study is to determine the predictive value of cytokine gene polymorphisms for the development of end-stage renal disease. (Babel et al., 2006).	1
Methods	4	Study design	Key elements presented earlier in the paper.	1
	5	Setting	Locations: Hospital of the researchers Relevant dates mentioned in the paper (Babel et al., 2006).	1
	6	Participants	Selection criteria availed.	1
	7	Variables	Outcomes and predictors are clearly defined.	1
	8	Data sources & measurements	Clearly stated.	1
	9	Bias	Mentioned but not analyzed.	0.5
	10	Study size	Study size provided.	1
	11	Quantitative variables	Clear.	1
	12	Statistical methods	Statistical methods are adhered.	1
Results	13	Participant	Study size is provided.	1
	14	Descriptive data	Demographic and clinical Missing data not mentioned.	0.5
	15	Outcome data	Outcome data-provided.	1
	16	Main results	Unadjusted estimates and adjusted estimates are provided.	1

	17	Other analysis	Sensitivity is fully analysed.	1
Discussion	18	Key results	Made clear.	1
	19	Limitations	Made clear.	1
	20	Interpretation	Provided.	1
	21	Generalizability	Made clear.	1
Other information	22	Source of funding and their role	Mentioned in the acknowledgement	1
	Total score			**21.0**

Table 4. 8 Predictive value of cytokine gene polymorphisms for the development of end-stage renal disease (Babel et al., 2006).

5. Discussion

The results obtained can be summarised in the table below.

No.	Name of article	Raw marks scored	Calculation	Percentage (%)
1	Genetics of diabetic nephropathy (Lee et al., 2005).	21.0	(21/22)*100	95,45
2	Journal of Diabetes and Its Complications (Gupta et al., 2015).	18.5	(18.5/22)*100	84,09
3	Association of of TGFβ1, TNFα, CCR2 and CCR5 gene polymorphisms (Prasad et al., 2007).	18.0	(18.0/22)*100	81,81
4	Association between LTA, TNF and AGER Polymorphisms and Late Diabetic Complications (Lindholm et al., 2008).	19.0	(19./22)*100	86,36
5	Association of interleukin-10 polymorphisms with cytokines in type 2 diabetic nephropathy. (Kung et al., 2010).	20	(20/22)*100	90,90
6	Gene (Dabhi and Mistry, 2015)	17.0	(17.0/22)*100	77,27
7	Genetic Determination of TNF and Myeloperoxidase Production in Dialyzed Patients with Diabetic Nephropathy (Buraczynska et al., 2004).	20.0	(20.0/22)*100	90,90
8	Predictive value of cytokine gene polymorphisms for the development of end-stage renal disease (Babel et al., 2006).	21.0	(21/22)*100	95,45

Table 5. 1 Results in summary

The results are grouped as shown in the table below for the purpose of analysis.

Grouping of data	0.00-24.99%	25.00-49.99%	50.00-74.99%	75.00-100%
Number of articles (frequency)	0	0	0	8

Table 5. 2 Grouped data

From the table of grouped data it is well depicted that all the journal articles analysed by the STROBE statement (checklist) lie in the fourth group of the table i.e. they have scores of 75% and above with half of the articles found to have scores over 90%.

Therefore, a general deduction can be made. The STROBE Statement has high reporting quality in case-controlled studies, as most of the articles that were assessed, satisfied the majority of the points on the STROBE checklist. Nonetheless, the deductions would have been much more reliable if a large sample population was analysed. The only limitations for analysing large sample populations is that it is time consuming since each article must be read and cross-checked with the STROBE Statement.

It is also important to reach a conclusion on the quality of the articles assessed. All eight articles, tend to converge towards a common point, i.e. they are nearly homogeneous in their findings. Since almost all of them state that there is no clear relationship between the TNF variant and diabetic nephropathy. But suggestions are made for further investigation to include a larger sample population, which can provide us with a clear representation as to the event rate in the general population. Therefore, it can be deduced that the articles assessed are of high quality because firstly their findings tend to converge at a point and secondly, they meet most requirements set forth in the STROBE statement.

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