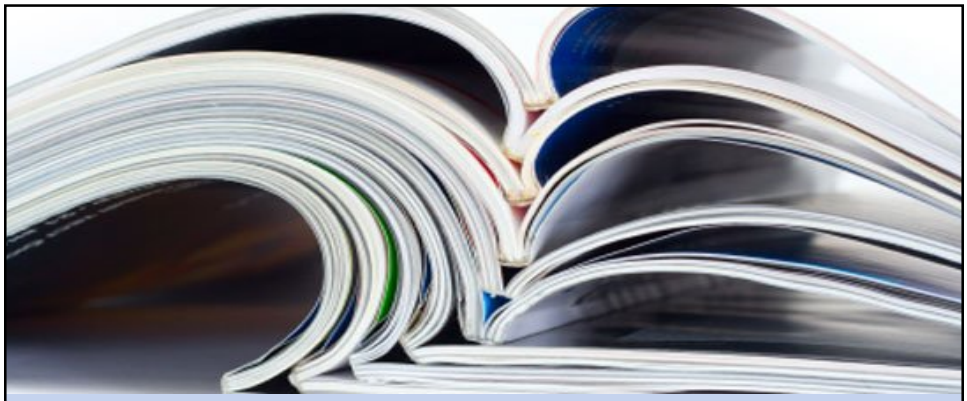


Types of academic/scholarly articles

By

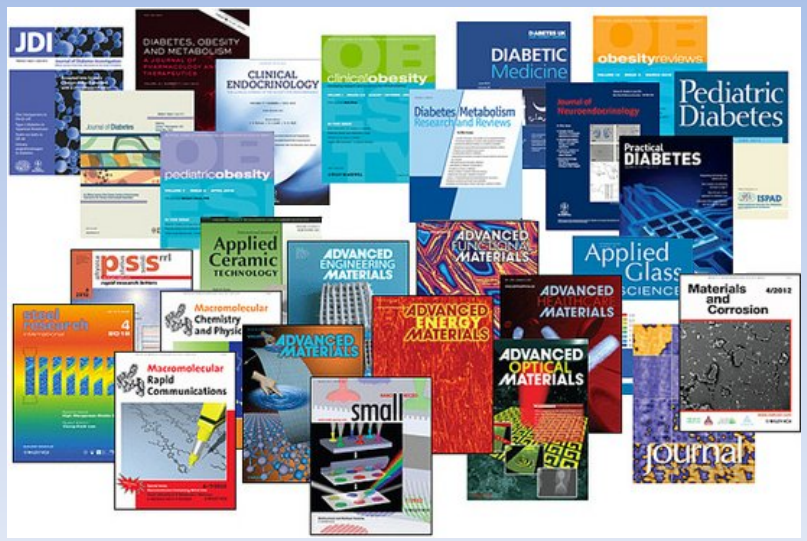
Zadeh-Vakili A, PhD

Research

Reading scientific literature

- A necessary component of research.
- The mean by which scientists communicate.
- Good examples of the scientific writing style.
- Enable you to find scientific literature on subjects of your interest.

How to Find the Best Sources to Cite for an Academic Paper

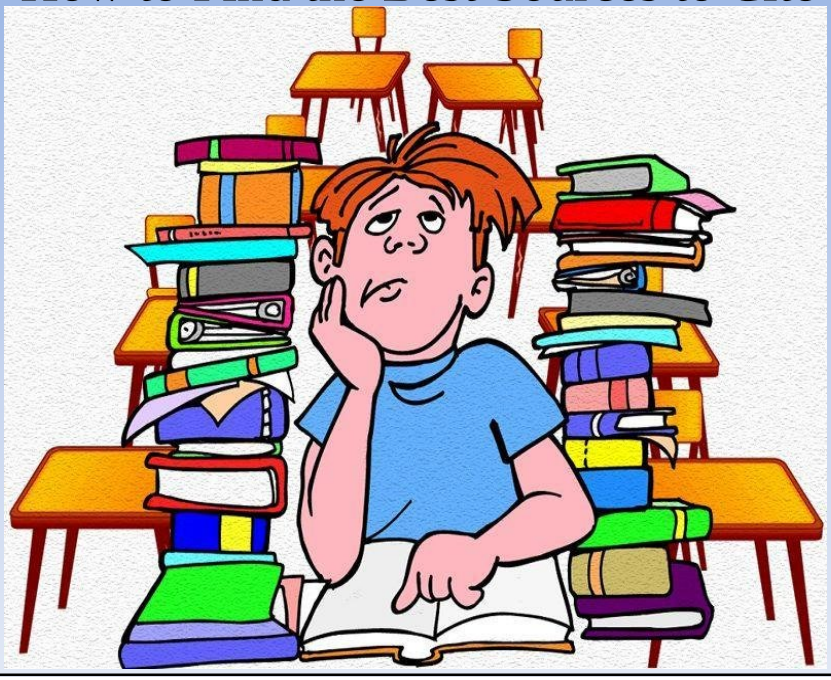


How to Find the Best Sources to Cite for an Academic Paper

Countless sources of information are available on any topic.

Which of these sources one should cite?

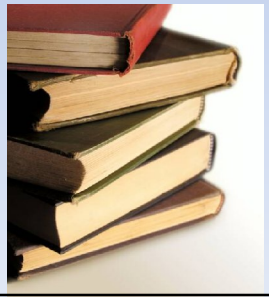
How to Find the Best Sources to Cite



Types of academic source

The most common forms of academic source are:

- Books
- Journal articles
- Published reports



What is an academic/scholarly article?

It has to pass an

academic quality assessment

This control process is called

peer-reviewing.

What Peer Review Is?

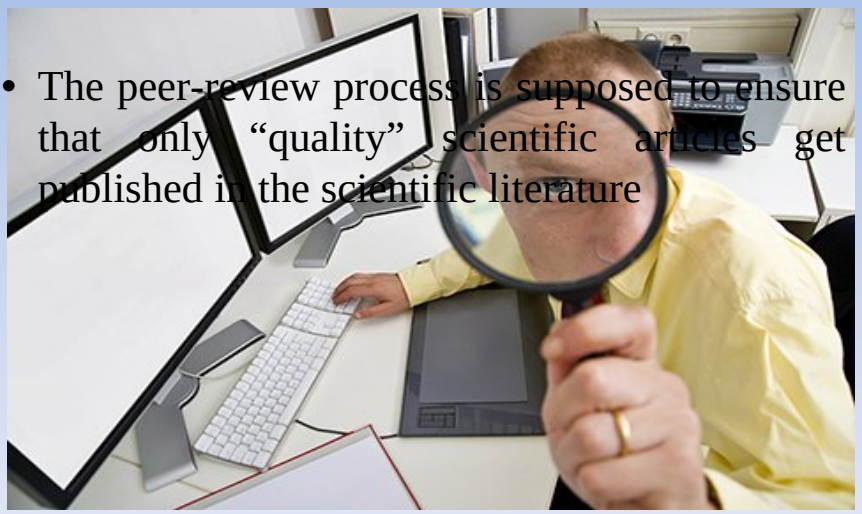
- Submitted article to a scientific journal, is generally reviewed by **people who are experts in the relevant subject** in order to determine **whether or not the article is worthy of publication**.

Peer Review

"Peer reviewers" determine:

- whether or not the paper's **conclusions are reasonable** based on the bulk of the data
- whether or not the conclusions and/or data are **novel or interesting enough** to merit publication

Peer Review



- The peer-review process is supposed to ensure that only "quality" scientific articles get published in the scientific literature

There are different types of academic/scholarly articles

- Research Article
- Case Report
- Review Article
- Meta-Analysis Article
- Letters or Communications
- Theoretical Article

Types of sources

- There are three main types of sources used in academic research:
- **Primary**
- **Secondary**
- **Tertiary**

Types of sources: Primary source

- A primary source is material produced by someone who was at the scene, event, or occurrence.

Types of sources: Secondary source

- Secondary sources are based on primary sources and are usually studies which analyze, evaluate, interpret or criticize primary sources.

Types of sources: Tertiary source

- Tertiary sources compile and condense information from other sources. They are meant to provide a broad introductory overview of a topic.

Characteristics of Articles

Type	Description
Research/Empirical	Article reporting on the results of one or more studies or experiments, written by the person(s) who conducted the research. This is considered one type of primary source.
Case Study	Detailed account of clinically important cases of common and rare conditions.
Review	Summarizes the findings of others studies or experiments; attempts to identify trends or draw broader conclusions. Scholarly in nature but not a primary source or research article, however its references to other articles will include primary sources or research articles.
Letters or Communications	Short descriptions of important latest study or research findings which are usually considered urgent for immediate publication. Examples: breakthroughs regarding cures or treatments for previously incurable conditions, or cure for a particular outbreak of disease, like for example swine flu.

Type	Description
Meta-Analysis	A meta-analysis is a mathematical synthesis of the results of two or more primary studies that addressed the same hypothesis in the same way.
Theoretical	Containing or referring to a set of abstract principles related to a specific field of knowledge; characteristically it does not contain original empirical research or present experimental data, although it is scholarly.

Zadeh-Vakili et al. Diabetology & Metabolic Syndrome 2011, 3:18
http://www.dmsjournal.com/content/3/1/18

DIABETOLOGY & METABOLIC SYNDROME

RESEARCH Open Access

Waist circumference and insulin resistance: a community based cross sectional study on reproductive aged Iranian women

Azita Zadeh-Vakili[1], Fahimeh R Tehrani[2*] and Farhad Hosseinpanah[1]

Abstract

Background: Although the positive relationship between insulin resistance (IR) and central obesity is well known, the direct relationship between waist circumference and IR is not clear yet and there is no consensus regarding the cut off value for waist circumference as a surrogate index for central obesity. The present study was aimed to determine the optimal cut-off value of waist circumference (WC) for predicting IR in reproductive aged Iranian women.

Methods: Using the stratified, multistage probability cluster sampling method 1036 women were randomly selected from among reproductive aged women of different geographic regions of Iran. Following implementation of exclusion criteria, complete data for 907 women remained for analysis. Insulin resistance was evaluated by the homeostasis model assessment (HOMA-IR) and its cut off value was defined as the 95th percentile of HOMA-IR value for 129 subjects, without any metabolic abnormality. The optimal cut-off of WC in relation to HOMA-IR was calculated based on the receiver operating characteristics (ROC) curve analysis using the Youden index and the area under curve (AUC).

Results: The mean age of the total sample of 907 subjects was 34.4 ± 7.6 years (range, 18 - 45 years). After adjustment for age the odds ratios (OR) of elevated HOMA-IR were progressively higher with increasing levels of waist circumference; the age adjusted OR of IR for women with WC > 95 cm in comparison to those subjects with WC < 80 cm, was 9.5 (95% CI 5.6-16.1). The optimal cutoff value for WC predicting IR was 88.5 cm, with a sensitivity and specificity of 71% and 64%, respectively.

Conclusions: Waist circumference is directly related to insulin resistance and the optimal cut-off value for waist circumference reflecting insulin resistance is considered to be 88.5 cm for reproductive aged Iranian women.

Keywords: Insulin resistance, Waist circumference, HOMA-IR, Cutoff, Iranian women

Background

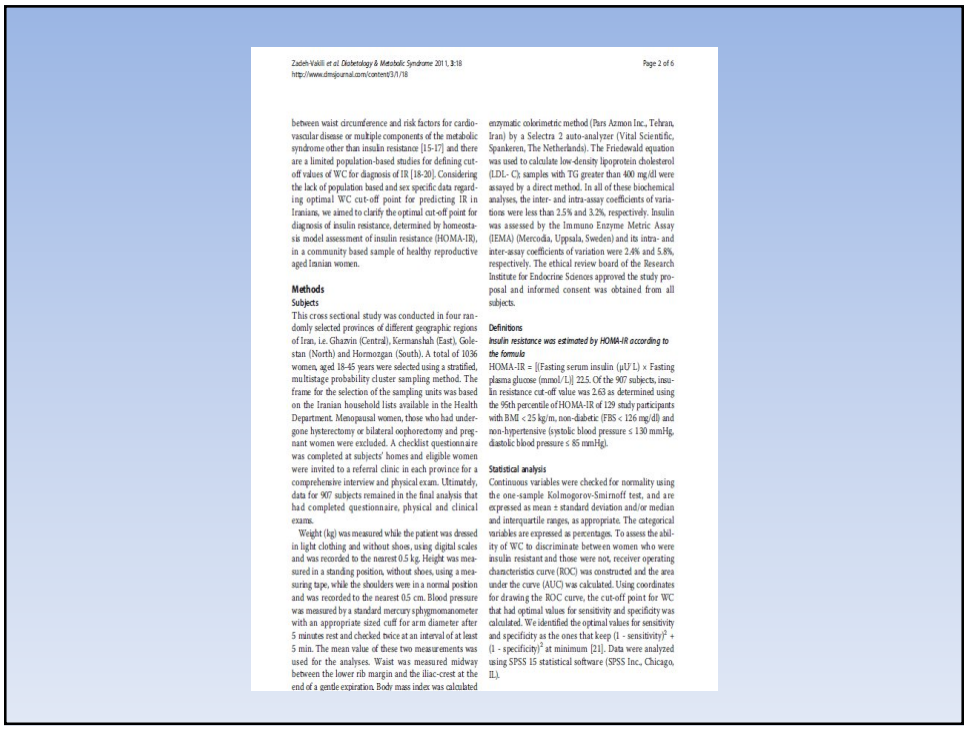
Insulin resistance (IR) is the main pathophysiological feature of the metabolic syndrome (MetS), which in turn leads to increased risk of cardiovascular disease [1,2]. Central obesity, main diagnostic criteria for the MetS, is considered to predispose individuals for insulin resistance [3-5]. Waist circumference (WC), the best anthropometric indicator of central obesity [6,7], is closely associated with IR and provides a rapid, inexpensive and non-invasive way of identifying the presence of IR [8-11].

The International Diabetes Federation (IDF) has declared that waist is a gender and ethnic-group specific indicator and has adopted different cut-offs for waist circumference in different ethnicities [12,13]. The cut-off points for Europides are 94 cm in men and 80 cm in women, while those for Chinese and South Asians are 90 cm in men and 80 cm in women [12]. For Iranians, based on both cross-sectional and longitudinal outcome based studies, the cut-off point of 95 cm for WC to diagnose MetS was identical in men and women [14,15]. However, these studies were primarily based on the relationship

* Correspondence: fahrehtehrani@endocrine.ac.ir
[2]Reproductive Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran
Full list of author information is available at the end of the article

BioMed Central

© 2011 Zadeh-Vakili et al; licensee BioMed Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/2.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.



between waist circumference and risk factors for cardiovascular disease or multiple components of the metabolic syndrome other than insulin resistance [15-17] and there are a limited population-based studies for defining cut-off values of WC for diagnosis of IR [18-20]. Considering the lack of population based and sex specific data regarding optimal WC cut-off point for predicting IR in Iranians, we aimed to clarify the optimal cut-off point for diagnosis of insulin resistance, determined by homeostasis model assessment of insulin resistance (HOMA-IR), in a community based sample of healthy reproductive aged Iranian women.

Methods

Subjects

This cross sectional study was conducted in four randomly selected provinces of different geographic regions of Iran, i.e. Ghazvin (Central), Kermanshah (East), Golestan (North) and Hormozgan (South). A total of 1036 women, aged 18-45 years were selected using a stratified, multistage probability cluster sampling method. The frame for the selection of the sampling units was based on the Iranian household lists available in the Health Department. Menopausal women, those who had undergone hysterectomy or bilateral oophorectomy and pregnant women were excluded. A checklist questionnaire was completed at subjects' homes and eligible women were invited to a referral clinic in each province for a comprehensive interview and physical exam. Ultimately, data for 907 subjects remained in the final analysis that had completed questionnaire, physical and clinical exams.

Weight (kg) was measured while the patient was dressed in light clothing and without shoes, using digital scales and was recorded to the nearest 0.5 kg. Height was measured in a standing position, without shoes, using a measuring tape, while the shoulders were in a normal position and was recorded to the nearest 0.5 cm. Blood pressure was measured by a standard mercury sphygmomanometer with an appropriate sized cuff for arm diameter after 5 minutes rest and checked twice at an interval of at least 5 min. The mean value of these two measurements was used for the analyses. Waist was measured midway between the lower rib margin and the iliac-crest at the end of a gentle expiration. Body mass index was calculated

enzymatic colorimetric method (Pars Azmon Inc., Tehran, Iran) by a Selectra 2 auto-analyzer (Vital Scientific, Spankeren, The Netherlands). The Friedewald equation was used to calculate low-density lipoprotein cholesterol (LDL- C); samples with TG greater than 400 mg/dl were assayed by a direct method. In all of these biochemical analyses, the inter- and intra-assay coefficients of variations were less than 2.5% and 3.2%, respectively. Insulin was assessed by the Immuno Enzyme Metric Assay (IEMA) (Mercodia, Uppsala, Sweden) and its intra- and inter-assay coefficients of variation were 2.4% and 5.8%, respectively. The ethical review board of the Research Institute for Endocrine Sciences approved the study proposal and informed consent was obtained from all subjects.

Definitions

Insulin resistance was estimated by HOMA-IR according to the formula

HOMA-IR = [(Fasting serum insulin (μU/L) × Fasting plasma glucose (mmol/L)] 22.5. Of the 907 subjects, insulin resistance cut-off value was 2.63 as determined using the 95th percentile of HOMA-IR of 129 study participants with BMI < 25 kg/m, non-diabetic (FBS < 126 mg/dl) and non-hypertensive (systolic blood pressure ≤ 130 mmHg, diastolic blood pressure ≤ 85 mmHg).

Statistical analysis

Continuous variables were checked for normality using the one-sample Kolmogorov-Smirnoff test, and are expressed as mean ± standard deviation and/or median and interquartile ranges, as appropriate. The categorical variables are expressed as percentages. To assess the ability of WC to discriminate between women who were insulin resistant and those were not, receiver operating characteristics curve (ROC) was constructed and the area under the curve (AUC) was calculated. Using coordinates for drawing the ROC curve, the cut-off point for WC that had optimal values for sensitivity and specificity was calculated. We identified the optimal values for sensitivity and specificity as the ones that keep $(1 - \text{sensitivity})^2 + (1 - \text{specificity})^2$ at minimum [21]. Data were analyzed using SPSS 15 statistical software (SPSS Inc., Chicago, IL).

Table 1 Characteristics of the study subjects (n = 907)

Variable	Value (means ± SD)
Age (Year)	34.4 ± 7.6
Systolic blood pressure (mmHg)	109 ± 14
Diastolic blood pressure (mmHg)	69.2 ± 11
Total cholesterol (mg/dl)	185 ± 42
LDL cholesterol (mg/dl)	111 ± 35
HDL cholesterol (mg/dl)	45 ± 13
Triglycerides (mg/dl)	142 ± 98
Weight (kg)	67.5 ± 12.8
Height (m)	159 ± 6
BMI (kg/m^2)	26.9 ± 5.1
Waist (cm)	85.0 ± 12.2
Hip (cm)	105 ± 11
Fasting plasma glucose (mg/dl)	88.9 ± 26.1
Fasting plasma insulin (UI/ml)	9.0 ± 9.1
HOMA	2.1 ± 2.8
Insulin resistance(%)	21.2*

*Percent of women with insulin resistance.

these risk factors except diastolic blood pressure were significantly higher among women with insulin resistance. The relationship between WC and HOMA-IR index is shown in Figure 1. There was a significant positive correlation between WC and HOMA-IR index ($r = 0.32$, $p < 0.001$).

The odds ratios (ORs) for having IR were increased according to WC categories. The age adjusted OR for having IR for women with WC > 95 cm in comparison to those subjects with WC < 80 cm, were 9.5 (95% CI 5.6-16.1) (Table 3).

Table 2 Characteristics of the study subjects according to the IR status (measured in terms of the HOMA value)

	With IR (n = 192)	Without IR (n = 715)	P-value
Age (Year)	34.9 ± 7.4	34.2 ± 7.7	0.256
Glucose (mg/dL)	106 ± 39	84.2 ± 18.2	< 0001
Insulin (UI/mL)	19.1 ± 15.5	6.3 ± 2.7	< 0001
HOMA	5.1 ± 5.1	1.29 ± 0.6	< 0001
Total cholesterol (mg/dL)	200 ± 47	180 ± 39	< 0001
LDL cholesterol (mg/dL)	120 ± 41	109 ± 33	< 0001
HDL cholesterol (mg/dL)	39.5 ± 14.2	46.5 ± 12.2	< 0001
Triglycerides (mg/dL)	201 ± 150	126 ± 70	< 0001

Figure 2 presents the ROC curves for the ability of the waist circumference to identify women with insulin resistance. Using the ROC curve analysis the optimal value for sensitivity and specificity that keep $(1 - \text{sensitivity})^2 + (1 - \text{specificity})^2$ at minimum was 88.5 cm. Sensitivity and specificity were 71% and 64%, respectively.

Discussion

In this population based cross sectional study we found that 88.5 cm is the optimal cut-off for predicting IR for reproductive aged Iranian women, our results indicating a significant, linear relationship between waist circumference and insulin resistance, measured by HOMA-IR. The odds ratio for the risk of insulin resistance using a cut-off < 80 cm for WC as a reference, increased progressively in proportion to the size of waist circumference.

Since insulin resistance is considered as an independent predictor for age related diseases, including cardiovascular disease, access to an accurate tool for measurement of the IR plays a vital role [22,23]. Although the euglycemic hyperinsulinemic clamp (Clamp-IR) is considered as the gold standard technique for estimation of insulin resistance, it is not applicable in epidemiologic studies. HOMA-IR, which is calculated from fasting plasma glucose (FPG) and insulin (FIRI), is highly correlated with the Clamp-IR; therefore it is a useful surrogate index of insulin resistance in both healthy and diabetic subjects [24-26]. Despite the wide use of HOMA-IR, no consensus has been reached regarding the HOMA-IR cut-off value for identifying subjects with IR. Lee et al. [27] and Radikova et al. [28] selected the 75th percentile of non-diabetic population for cut-off point of IR which corresponded with HOMA-IR values of 3.04 and 2.29 respectively. However, Ascaso et al defined insulin resistance as a HOMA index > 3.8, corresponding to the 90th percentile of the distribution in a healthy adult Spanish population [29]. The threshold values of HOMA-IR to determine IR, in an Iranian population (aged 20-77 years), using the lower limit of the top quintile of HOMA-IR distribution values in normal subjects, was defined as 1.78 (1.69 for men and 1.81 for women); additionally, racial and ethnic variability in the HOMA-IR cut points to diagnose IR is probable [30,31]. Therefore, to implement the HOMA-IR method successfully, it is important to define specific cut-points for the race or age of the studied population. In the pre-

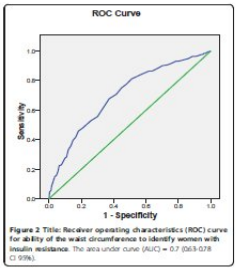


Figure 2 Title: Receiver operating characteristics (ROC) curve for ability of the waist circumference to identify women with insulin resistance. The area under curve (AUC) = 0.7 (0.63-0.78 CI 95%).

intra-assay variability in our data is also likely to be minimal because all the laboratory measurements were done at the same laboratory by the same person. The educational status and the prevalence of obesity in the present study was the same as that reported in a national study [39] and hence could justify and confirm our population as being representative of reproductive aged Iranian women. However as a main limitation we did not use gold standard technique for assessment of insulin resistance.

Conclusions

In conclusion, our results revealed that 88.5 cm is the optimal cut off proposed for predicting IR for Iranian reproductive aged women. A comprehensive study for evaluation of the correlation between the values of HOMA-IR and Clamp-IR among reproductive aged women is suggested.

Acknowledgements
We are indebted to each of the study participants for the substantial time and effort contributed to this study. Acknowledgments are also due to the research staff at the health department of Ghaleh, Golestan, Kermanshah and Hormozgan provinces. My special thanks to Dr. M. Tohidi for her important contribution on testing and to Ms. N. Shiva for language editing of the manuscript and also to Dr. F. Azizi for his critical revision of the manuscript. The authors also thank the National Council of Scientific Research of the I.R. Iran for the approval and founds of this national research project.

Author details
[1]Obesity Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran. [2]Reproductive Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Authors' contributions
AZ contributes in execution, analysis, manuscript drafting and critical discussion. PT contributes in study design, execution, analysis, manuscript drafting and critical discussion. FH contributes in analysis and manuscript drafting. All authors read and approved the final manuscript.

Competing interests
The authors declare that they have no competing interests.

Received: 5 April 2011 Accepted: 10 August 2011
Published: 10 August 2011

References

1. Cornier MA, Dabelea D, Hernandez TL, Lindstrom RC, Steig AJ, Stob NR, Van Pelt RE, Wang H, Eckel RH: **The metabolic syndrome.** *Endocr Rev* 2008, **29**:777-822.
2. Fernandez E, Haffner SM, Mitchell BD, Stern MP: **Hyperinsulinemia: the key feature of a cardiovascular and metabolic syndrome.** *Diabetologia* 1991, **34**:416-422.
3. Saaristo TE, Barengo NC, Korpi-Hyovalti E, Oksa H, Puolijoki H, Saltevo JT, Vanhala M, Sundvall J, Saaristo L, Peltonen M, Tuomilehto J: **High prevalence of obesity, central obesity and abnormal glucose tolerance in the middle-aged Finnish population.** *BMC Public Health* 2008, **8**:423.
4. Lord J, Thomas R, Fox B, Acharya U, Wilkin T: **The central issue? Visceral fat mass is a good marker of insulin resistance and metabolic disturbance in women with polycystic ovary syndrome.** *BJOG* 2006, **113**:1203-9.
5. Peter G, Kopelman IDC, William H: **Dietz Clinical Obesity in Adults and Children.** Singapore: WileyBlackwell, 3 2009, 512.
6. Taylor RW, Jones IE, Williams SM, Goulding A: **Evaluation of waist circumference, waist-to-hip ratio, and the conicity index as screening tools for high trunk fat mass, as measured by dual-energy X-ray absorptiometry, in children aged 3-19 y.** *Am J Clin Nutr* 2000, **72**:490-5.
7. Rankinen T, Kim SY, Perusse L, Despres JP, Bouchard C: **The prediction of abdominal visceral fat level from body composition and anthropometry: ROC analysis.** *Int J Obes Relat Metab Disord* 1999, **23**:801-9.
8. Lee JM, Okumura MM, Wickrad SJ, Gurney JG: **Waist circumference percentile thresholds for identifying adolescents with insulin resistance in clinical practice.** *Pediatr Diabetes* 2009, **10**:336-42.
9. Rodriguez-Rodriguez E, Palmeros-Exsome C, Lopez-Sobaler AM, Ortega RM: **Preliminary data on the association between waist circumference and insulin resistance in children without a previous diagnosis.** *Eur J Pediatr* 2011, **170**:53-61.
10. Gilon N, Pär H, Tommy J, Ingemar L, Åke T, Rosanne F, John Ö: **Waist circumference alone predicts insulin resistance as good as the metabolic syndrome in elderly women.** *European journal of internal medicine* 2008, **19**:503-526.
11. Wahrenberg H, Hertel K, Leijonhufvud BM, Persson LG, Toft E, Arner P: **Use of waist circumference to predict insulin resistance: retrospective study.** *BMJ* 2005, **330**:1363-4.
12. Alberti K, Zimmet P, Shaw J: **The metabolic syndrome--a new worldwide definition.** *Lancet* 2005, **366**:1059-1062.
13. Alberti K, Eckel R, Grundy S, Zimmet P, Cleeman J, Donato K, Fruchart J, James W, Loria C, Smith S: **Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity.** *Circulation* 2009, **120**:1640-1645.
14. Azizi F, Hadaegh F, Khalili D, Esteghamati A, Hosseinpanah F, Delavari A, Saiedi S, Meysamie F, Zabetian A, Mehrabi Y, Kelishadi R, Aghajani H: **Appropriate definition of metabolic syndrome among Iranian adults: report of the Iranian National Committee of Obesity.** *Arch Iran Med* 2010, **13**:426-8.
15. Delavari A, Forouzanfar MH, Alikhani S, Sharifian A, Kelishadi R: **First nationwide study of the prevalence of the metabolic syndrome and optimal cutoffs points of waist circumference in the Middle East: the**

Evaluating Your Information

No matter where your information comes from, you should look at it critically and consider the following:

- Is the author qualified to write on the topic?
- Is the information scholarly?
- Is it current?
- Is the information accurate? Has it been edited by other experts? Has the author provided references?
- Is the information objective or is there an obvious bias?
- Is the information relevant to your topic?
- Do you have enough information to cover all aspects of your topic?

USE PRIMARY LITERATURE FOR:
For most science course assignments you are expected to base your work on the primary scientific literature.
Do not refer to a study that you are ready ABOUT in a primary source, but that you have not read yourself. This is NOT an acceptable procedure. You should make all efforts to read the additional study itself.
USE SECONDARY LITERATURE FOR:
Secondary literature is useful for gaining a broad perspective on a topic or a synthesis of ideas about a topic and to find a bibliography of relevant sources
Secondary literture can be used in addition to primary literture, but not in place of it. for instance, if you are reading a review article which refers to information in a primary research article, you should find that primary article and read it yourself

Types of Sources for a Research Paper

- There are two types of research that can be incorporated into a paper: primary and secondary. Most students rely heavily on secondary research, which involves looking at other people's thoughts on a subject, either in books or on the Web. Primary research involves collecting data yourself, through personal interviews, observations or surveys. Knowing about the different types of research you can use helps you determine what type will make your research paper stronger.

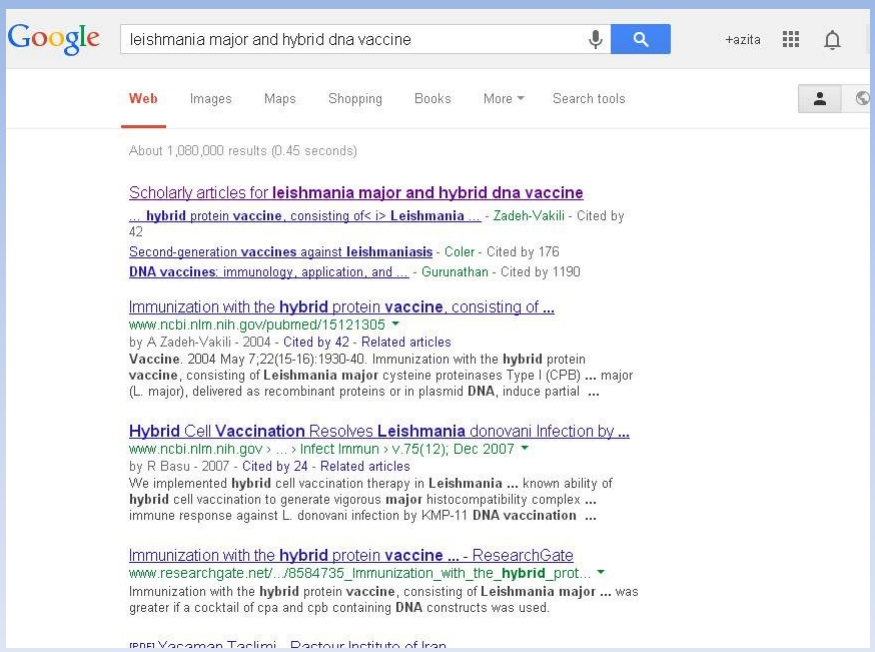
- They come in the form of systematic reviews and literature reviews and are a form of secondary literature.[4] Systematic reviews determine an objective list of criteria, and find all previously published original experimental papers that meet the criteria. They then compare the results presented in these papers. Literature reviews, by contrast, provide a summary of what the authors believe are the best and most relevant prior publications.

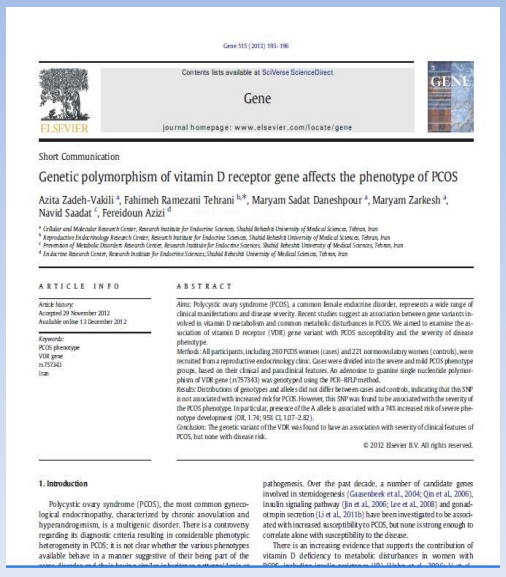
- c
- News, Book Reviews, Opinion, Letters to the Editor, etc.
-
- Smith, G. (2009, August). Editorial: The need for complementary and alternative medicine familiarisation in undergraduate nurse education. *Journal of Clinical Nursing*. pp. 2113-2115.
- Theoretical Article

- Green, C. (2009). A comprehensive theory of the human person from philosophy and nursing. *Nursing Philosophy*, *10*(4), 263-274.
- Review Article
- Parker, M., & Thorslund, M. (2007, April). Health trends in the elderly population: Getting better and getting worse. *Gerontologist*, *47*(2), 150-158.
- Research Article
- Gril, B., Palmieri, D., Bronder, J. L., Herring, J. M., Vega-Valle, E., Feigenbaum, L., & ... Steeg, P. S. (2008). Effect of lapatinib on the outgrowth of metastatic breast cancer cells to the brain. *JNCI: Journal of the National Cancer Institute*, *100*(15), 1092-1103.

There are different types of academic/scholarly articles

Type	Definition
News, Book Reviews, Opinion, Letters to the Editor, etc.	•Scholarly journals will publish some types of articles that are not peer reviewed or based on research. **Remember that not every article in peer reviewed journals is a peer-reviewed research article.** **•OK for Class Assignment? NO**
Theoretical Article	•An article containing or referring to a set of new or established abstract principles related to a specific field of knowledge; **normally does not contain original research or present experimental data**, although it is scholarly. **•OK for Class Assignment? NO**
Review Article	•An article summarizing the results of studies or experiments, often attempting to identify trends or draw broader conclusions. Although **scholarly, it is not considered a primary source or research article itself**, but it may reference other primary sources or research articles. **•OK for Class Assignment? NO**
Research Article	**•An article reporting on the results of one or more empirical studies or experiments, written by the person(s) who conducted the research.** Look in the title or abstract for words like *study, research, measure, subjects, data, effects, survey,* or *statistical* which might indicate empirical research. **•OK for Class Assignment? YES**





Gene 515 (2013) 193–196

Contents lists available at SciVerse ScienceDirect

Gene

journal homepage: www.elsevier.com/locate/gene

Short Communication

Genetic polymorphism of vitamin D receptor gene affects the phenotype of PCOS

Azita Zadeh-Vakili [a], Fahimeh Ramezani Tehrani [b,*], Maryam Sadat Daneshpour [a], Maryam Zarkesh [a], Navid Saadat [c], Fereidoun Azizi [d]

[a] Cellular and Molecular Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[b] Reproductive Endocrinology Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[c] Prevention of Metabolic Disorders Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[d] Endocrine Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran

ARTICLE INFO

Article history:
Accepted 29 November 2012
Available online 13 December 2012

Keywords:
PCOS phenotype
VDR gene
rs757343
Iran

ABSTRACT

Aims: Polycystic ovary syndrome (PCOS), a common female endocrine disorder, represents a wide range of clinical manifestations and disease severity. Recent studies suggest an association between gene variants involved in vitamin D metabolism and common metabolic disturbances in PCOS. We aimed to examine the association of vitamin D receptor (VDR) gene variant with PCOS susceptibility and the severity of disease phenotype.

Methods: All participants, including 260 PCOS women (cases) and 221 normoovulatory women (controls), were recruited from a reproductive-endocrinology clinic. Cases were divided into the severe and mild PCOS phenotype groups, based on their clinical and paraclinical features. An adenosine to guanine single nucleotide polymorphism of VDR gene (rs757343) was genotyped using the PCR–RFLP method.

Results: Distributions of genotypes and alleles did not differ between cases and controls, indicating that this SNP is not associated with increased risk for PCOS. However, this SNP was found to be associated with the severity of the PCOS phenotype. In particular, presence of the A allele is associated with a 74% increased risk of severe phenotype development (OR, 1.74; 95% CI, 1.07–2.82).

Conclusion: The genetic variant of the VDR was found to have an association with severity of clinical features of PCOS, but none with disease risk.

© 2012 Elsevier B.V. All rights reserved.

1. Introduction

Polycystic ovary syndrome (PCOS), the most common gynecological endocrinopathy, characterized by chronic anovulation and hyperandrogenism, is a multigenic disorder. There is a controversy regarding its diagnostic criteria resulting in considerable phenotypic heterogeneity in PCOS; it is not clear whether the various phenotypes available behave in a manner suggestive of their being part of the

pathogenesis. Over the past decade, a number of candidate genes involved in steroidogenesis (Gaszenbeek et al., 2004; Qin et al., 2006), insulin signaling pathway (Jin et al., 2006; Lee et al., 2008) and gonadotropin secretion (Li et al., 2011b) have been investigated to be associated with increased susceptibility to PCOS, but none is strong enough to correlate alone with susceptibility to the disease.

There is an increasing evidence that supports the contribution of vitamin D deficiency to metabolic disturbances in women with

Blood Cells, Molecules, and Diseases 43 (2009) 158–160

Contents lists available at ScienceDirect

Blood Cells, Molecules, and Diseases

journal homepage: www.elsevier.com/locate/ybcmd

Letter to the Editor

Molecular characterization of thalassemia intermedia, due to co-inheritance of homozygous alpha triplication and IVSI-5 β-thalassemia

To the editor,

Thalassemia intermedia is referred to a group of patients who are affected with a less severe form of the disease when compared with thalassemia major. Patients may present with diverse pathology, however, the most accepted definition is that, a patient may start to become transfusion-dependent later in life (after the age of three). They are either transfusion independent or require transfusion at longer intervals than monthly [1]. The clinical severity of the disease is associated with the degree of α/non-α chain imbalance [1]. This phenotype may be caused by interaction of an only one β-globin gene defect along with an excessive α-globin gene expression as a result of the alpha triplication. Here we describe a child with thalassemia intermedia phenotype due to homozygote alpha triplication ($\alpha\alpha\alpha^{anti\ 3.7}/\alpha\alpha\alpha^{anti\ 3.7}$) and a β-globin gene mutation (IVSI-5).

A relative (1st cousin) couple from Nehbandan, Sistan and Baloochestan province, south-east of Iran with an affected child came for pre-pregnancy genetic counseling. The father was a carrier of β-thalassemia minor with IVSI-5 mutation and his wife was hematologically normal and had no mutation in her β-globin genes. The propositus, a 4 year old girl showed mild thalassemic facise, palpable spleen, and a moderately severe chronic anemia with microcytosis, hypochromia, anisopoikilocytosis, schistocyte and tear drop cells in the blood since the age of two (Table 1). Glucose 6-phosphate dehydrogenase (G6PD) enzyme activity showed G6PD deficiency. This child had only been transfused once for her anemia, which could have been due to her G6PD deficiency. Her father had a typical β-thalassemia carrier phenotype on blood examination. On the other hand her mother showed normal hematological parameters. Their

to occur more often. Its co-inheritance with β-thalassemia may adversely affect the hematological picture of β-thalassemia carriers. When β-thalassemia carriers, have relatively excess α-globin chains, it may result in a condition similar to β-thalassemia intermedia phenotype [4].

The alpha 3.7 kb deletion is the most frequent α-globin mutation in Iran and it contributes to about 60% of α-thalassemia alleles [3,5]. One would then expect that the $anti^{3.7}$ triplication is common in Iran as well. Since, the frequency of β-thalassemia gene is close to 10% in some southern parts of Iran (including Sistan and Balouhestan); one would expect to see frequent co-inheritance of alpha triplication with β-thalassemia. Our personal observations do not, however, support this claim. Reported frequency of $anti^{3.7}$ triplication is 0.38% in American blacks, less than 0.4% in Sardinians and 5% in Greek Cypriots [6]. The reason could be that we are only seeing transfusion-dependent patients, whereas persons with β-thalassemia mutation with alpha triplication may have milder phenotypes, like thalassemia intermedia as indicated below. However, this discrepancy in the frequency of the single α-globin gene compared to the $anti^{3.7}$ triplication genotype might be due to the selective benefit of the former genotype [6]. In addition, in spite of several reports from other populations, hematological parameters and the clinical picture for people carrying both β-thalassemia and α-triplication mutations still remain to be well defined [7]. The presence of extra α-globin gene can worsen the effects of already imbalanced α/β chain ratio caused by a defective β-globin gene [1,8]. However, there are no consistent clinical and hematologic abnormalities in these cases [6] (Table 2) and they can range from asymptomatic presentation to mild and moderate thalassemia intermedia phenotypes [1]. One reason for this may be the co-inheritance of alpha triplication with different types of β-globin mutation (as it is usually referred to β^{o} and β^{+}).

One can expect to see the presence of two copies of $anti^{3.7}$ triplication when both parents are carriers of alpha triplication. However, this may be very rare in populations which consangui-

IJMS
Vol 33, No 1, March 2008

Original Article

Efficiency of *BclI* Restriction Fragment Length Polymorphism for Detection of Hemophilia A Carriers in Sistan and Baluchestan Province, Southeast of Iran

A. Zaeh-Vakili, P. Rahgh[1], Gh. Rastegar Lari[2]

Department of Genetics, Thalassemia Prenatal Diagnosis Center, Zahedan University of Medical sciences, Zahedan, Iran.
[1]Department of Pediatrics Hematology-Oncology, Mofid Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
[2]Department of Hematology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran.

Correspondence:
Azita Zaeh-Vakili PhD,
Ali-e-Asghar Hospital,
Thalassemia Prenatal Diagnosis Center,
Zahedan University of Medical sciences,
Zahedan, Iran.
Tel/Fax: +98 541 3218998
Email: Azitavakili@gmail.com

Abstract

Background: Indirect genetic diagnosis using polymorphic DNA markers can detect carriers of hemophilia A. This technique is preferable in developing countries because of its simplicity and cost effectiveness compared to direct mutation analysis. In the present study, we examined usefulness of intragenic marker *BclI* restriction fragment length polymorphism (RFLP) at intron 18, for carrier detection. How this marker is informative was tested in 102 members of 16 hemophiliac families from Sistan and Baluchestan province, Southeast of Iran.

Methods: Blood samples were obtained from 29 hemophilia A patients and 73 of their relatives, after taking informed consents. DNA was extracted using proteinase K digestion followed by DNA precipitation. Factor VIII gene polymorphism was identified by the polymerase chain reaction/RFLP which is both sensitive and economical.

Results: Our results showed that almost 69.8% of X-chromosomes had restriction site for *BclI* enzyme. The heterozygosity rate for *BclI* polymorphism in tested women was 61.4%, signifying the usefulness of this marker in carrier detection. The informative rate respecting this polymorphism was 43.7% meaning that a remarkable percent of families from the target population could be diagnosed using this marker alone.

Conclusion: In Sistan and Baluchestan province where there is limited access to sophisticated facilities of molecular diagnosis, use of PCR-based analysis of DNA polymorphism in the *BclI* locus can be used to identify a remarkable percentage of the carriers and even for prenatal diagnosis. Meanwhile, it is necessary to evaluate the effectiveness of other polymorphic DNA markers to enhance the informative rate.
Iran J Med Sci 2008; 33(1): 33-36.

Keywords • Hemophilia A • RFLP • carrier detection • Iran

Introduction

Hemophilia A, an X-linked recessive disorder, is characterized by a deficiency in the activity of coagulation factor VIII. Generally, substitution therapy with factor

Reproduction (2002) **124**, 601–609

Review

Regulation of ovarian function: the role of anti-Müllerian hormone

Alexandra L. L. Durlinger, Jenny A. Visser and Axel P. N. Themmen

Department of Internal Medicine, Erasmus MC, PO Box 1738, 3000 DR Rotterdam, The Netherlands

Anti-Müllerian hormone (AMH), also known as Müllerian inhibiting substance, is a member of the transforming growth factor β superfamily of growth and differentiation factors. In contrast to other members of the family, which exert a broad range of functions in multiple tissues, the principal function of AMH is to induce regression of the Müllerian ducts during male sex differentiation. However, the patterns of expression of AMH and its type II receptor in the postnatal ovary indicate that AMH may play an important role in ovarian folliculogenesis. This review describes several *in vivo* and *in vitro* studies showing that AMH participates in two critical selection points of follicle development: it inhibits the recruitment of primordial follicles into the pool of growing follicles and also decreases the responsiveness of growing follicles to FSH.

In 1947 it was shown that during development of the male fetus a testicular factor distinct from testosterone caused regression of the Müllerian ducts, which form the anlagen of the female genital tract (Jost, 1947; Munnsterberg and Lowell-Badge, 1991). This factor was called anti-Müllerian hormone (AMH) and was subsequently identified as a dimeric glycoprotein related to transforming growth factor β (TGFβ) (Cate *et al.*, 1986). Together with inhibins, activins, bone morphogenetic proteins (BMPs), and growth and differentiation factors (GDFs), AMH is part of the TGFβ superfamily of peptide growth and differentiation factors (Massagué, 1990). Members of this family have a broad range of functions in mesenchymal–epithelial interactions, cell growth, extracellular matrix production and tissue remodelling (Massagué and Chen, 2000). In men, strong AMH expression is found in Sertoli cells from the moment of testicular differentiation during fetal development up to puberty, whereas in women AMH is produced by ovarian granulosa cells from about Smad proteins (for a review, see Massagué and Chen, 2000).

The type II receptor for AMH (AMHRII) was cloned several years ago (rat: Baarends *et al.*, 1994; rabbit: di Clemente *et al.*, 1994a). Expression of AMHRII mRNA was found in the mesenchymal cells surrounding the Müllerian ducts (Baarends *et al.*, 1994) and, in addition, in fetal and adult gonads of both sexes. Generation of AMHRII-deficient mice proved that this type II receptor is essential for AMH signalling, as demonstrated by the lack of Müllerian duct regression in AMHRII-deficient male mice (Mishina *et al.*, 1996). In addition, the relevance of this receptor to AMH action was further demonstrated by the identification of mutations in the AMHRII gene of patients with persistent Müllerian duct syndrome (PMDS) (Imbeaud *et al.*, 1996; Josso *et al.*, 1997).

More insight into the identity of the AMH type I receptor has been gained recently. Members of the TGFβ family can

Case Report 300

Charcot-Marie-Tooth Disease Type 1A: A Clinical, Electrophysiological, Pathological, and Genetic Study

Shiang-Yao Hsieh, MD; Hung-Chou Kuo, MD; Chun-Che Chu, MD; Kon-Ping Lin†, MD; Chin-Chang Huang, MD

Various clinical manifestations, electrophysiological findings, and sural nerve biopsies are reported in a Taiwanese family with type 1A Charcot-Marie-Tooth disease (CMT-1A). In addition, molecular genetic studies for duplication of the peripheral myelin protein 22 (PMP22) gene were also performed. There were 3 patients (2 men and 1 woman) with ages at onset ranging from 37 to 44 years. The onset of symptoms was insidious, and the neurological manifestations included distal muscle weakness and wasting, mild sensory loss, and hyporeflexia or areflexia. The severity of clinical manifestations varied from mild to severe, although with very prominent demyelinating polyneuropathy in electrophysiological studies. The sural nerve biopsy study revealed demyelination and an onion-bulb appearance. The molecular genetic studies confirmed duplication of the PMP22 gene in chromosome 17p11.2-12. We conclude that the clinical presentations, electrophysiological studies, and pathological studies as well as the molecular genetic analysis remain important in the clinical diagnosis of CMT-1A. (*Chang Gung Med J 2004;27:300-6*)

Key words: **Charcot-Marie-Tooth type 1A, peripheral myelin protein 22, demyelination, onion-bulb, molecular genetic study, neuropathology.**

Charcot-Marie-Tooth (CMT) disease, also called hereditary motor and sensory neuropathy (HMSN), is a common genetic disorder of peripheral neuropathy with an incidence of about 1 in 2500 persons.[1] The clinical phenotypes of all forms of CMT are generally similar and manifest as distal muscle weakness with a reversed champagne bottle, pes cavus, peroneal muscle wasting, claw hands with intrinsic hand muscle wasting, a decrease or absence of tendon reflexes, and sensory impairments.[2] In addition, there is a wide range of variation among the various types of CMT or even in the same type. Although a clinical diagnosis of CMT is seldom difficult, the different types of CMT cannot be differentiated by clinical features.

Discrimination of CMT1 (HMSN I) and CMT2 (HMSN II) is based on electrophysiological and neuropathological findings.[3,4] CMT1 is characterized by marked slowing of the nerve conduction velocity (NCV) and hypertrophic nerves due to repeated segmental demyelination and remyelination with onion-bulb formations,[4,5] while CMT2 is characterized by only a mild decrease in the motor NCV (MNCV) with axonal degeneration and regeneration in neuropathological studies.[6] Further subdivision is mainly based on genetic findings.

Recently, molecular genetic studies have demonstrated a duplication of the chromosome 17p11.2-12 region containing a dosage-sensitive gene, peripheral myelin protein 22 (PMP 22), in 60%-90% of all CMT-1A patients.[4,5] Affected patients carry 3 copies of PMP 22, and a gene-

From the Department of Neurology, Chang Gung Memorial Hospital, and University, Taipei; †Neurological Institute, Veterans General Hospital, Taipei.
Received: Mar. 18, 2003; Accepted: Jul. 25, 2003.
Address for reprints: Dr. Chin-Chang Huang, Department of Neurology, Chang Gung Memorial Hospital. 5, Fushing Street, Gueishan Shiang, Taoyuan, Taiwan 333, R.O.C. Tel.: 886-3-3281200 ext. 8418; Fax: 886-3-3287226; E-mail: cch6573@adm.cgmh.org.tw

- The review papers can be included in the introduction section, where general lay-out of the problem is presented. Original articles can be included in those sections of my paper where pin-pointed comparison or comments are required
- If author want to refer to a detailed work, original articles should be preferred. But if there is need to refer to only outline of work, review article should be preferred.

- In academic publishing, letters to the editor of an academic journal are usually open postpublication reviews of a paper, often critical of some aspect of the original paper. The authors of the original paper sometimes respond to these with a letter of their own. Controversial papers in mainstream journals often attract numerous letters to the editor. Good citation indexing services list the original papers together with all replies

- Why should you write a letter to the editor
- You think that an issue is so important that you have to speak out
- Part of your group's strategy is to persuade others to take a specific action
- Or you want to:
- Suggest an idea to others
- Influence public opinion
- Educate the general public on a specific matter
- Influence policy-makers or elected officials directly or indirectly
- Publicize the work of your group and attract volunteers or program participants

- letter to the editor provides a means of communication between the author of an article and the reader of a journal, allowing continued dialog about journal content to take place. Although not original research per se, a letter may provide new insight, make corrections, offer alternate theories, or request clarification about content printed in the journal. By providing additional information, the evidence may be strengthened. This paper provides first time writers some insight into the process of writing a letter to the editor.

short communication paper

- Some time there is important information that dilute the main information related to the research principal objectives. Therefore we omit it from the published paper. If one think that the omited information is important but cannot serve as the content of a full paper then it is worth to include that information in a short communication

- A Short Communication is suitable for recording the results of complete small investigations or giving details of new models or hypotheses, innovative methods, techniques or apparatus. The style of main sections need not conform to that of full-length papers. Short communications are 2 to 4 printed pages (about 6 to 12 manuscript pages) in length.

Types of articles

Three types of manuscripts can be submitted:

Regular articles: These should include new topics and add new information to recent and previous findings. Experimental procedures should be well detailed and lucid for others to verify the work. The length of a full paper should be the minimum required to describe the work.

Short Communications: these are meant for the results of complete small investigations or giving details of new models or hypotheses, innovative methods, techniques or apparatus. The style of main sections need not conform to that of full-length papers. Short communications are 2 to 4 printed pages (about 6 to 12 manuscript pages) in length.

Review: reviews and perspectives covering various topics are welcomed and encouraged. Reviews should be precise and not more than 4-6 printed pages (about 12 to 18 manuscript pages). Reviews manuscripts are also given to different qualified reviewers.

Review Process

All manuscripts are reviewed by an editor and members of the Editorial Board or qualified outside reviewers. This is done within the shortest given time. The journal, above all, strives to return reviewers' comments to authors within 3 weeks. The editorial board re-review manuscripts that are accepted until they are revised.

Kozal MJ (2009). Drug-resistant human immunodeficiency virus. Clin. Microbiol Infect. Suppl 1: 69-73.

Short Communications

Short Communications usually contain two figures and one table. They deal with work that has limited in scope than is found in full-length papers. The differences between full length papers and short communication are: (1) Abstracts are limited to 100 words; (2) instead of a separate Materials and Methods section, experimental procedures may be incorporated into Figure Legends and Table footnotes; (3) Results and Discussion should be combined into a single section.

Fees and Charges: There are no page charges or extra charges for colour photographs. Authors are charged a $450 handling fee. Publication of an article in the Information Technology Research Journal is not dependent upon the author's ability to pay the charges. Neither is acceptance to pay the handling fee a guarantee that the paper will be accepted for publication. Authors may still request (in advance) that the editorial office waive some of the handling fee under special circumstances.

- Regular articles: These should describe new and carefully confirmed findings, and experimental procedures should be given in sufficient detail for others to verify the work. The length of a full paper should be the minimum required to describe and interpret the work clearly.

- Reviews: Submissions of reviews and perspectives covering topics of current interest are welcome and encouraged. Reviews should be concise and no longer than 4-6 printed pages (about 12 to 18 manuscript pages). Reviews are also peer-reviewed.

- Review articles are an attempt to summarize the current state of understanding on a topic.[1] They analyze or discuss research previously published by others, rather than reporting new experimental results.[2][3]
- They come in the form of systematic reviews and literature reviews and are a form of secondary literature.[4] Systematic reviews determine an objective list of criteria, and find all previously published original experimental papers that meet the criteria. They then compare the results presented in these papers. Literature reviews, by contrast, provide a summary of what the authors believe are the best and most relevant prior publications.
- Some academic journals likewise specialize in review of a field; they are known as review journals.
- The concept of "review article" is separate from the concept of peer-reviewed literature. It is possible for a review to be peer-reviewed, and it is possible for a review to be non-peer-reviewed.
- WIKI

Peer Reviewed Articles

- Peer reviewed articles (or refereed articles or "primary literature") primarily appear in academic, scientific or other scholarly publications and are judged by an impartial panel of two or more experts in the field. The judgment criteria for any peer review article varies depending on the publication and subject matter, but peer reviewers (or referees) primarily focus on ensuring that an article is factually accurate, provides new information in a specified field and meets the proofreading and editorial guidelines of the publication.

- Questions to ask when reading and interpreting scholarly articles:
- What is the source (journal) of the article?
- Was the article peer reviewed?
- Who are the authors and what are their affiliations?
- What is the main subject of the study?
- What was the problem(s) investigated?
- What is purpose of rationale for the study?
- Who or what constituted the sample of population?
- What was the design of the study?
- What are the statistical analyses used?
- What are the results?
- Are the results clear?
- Did the results answer the identified questions?
- Do the results seem valid?
- Are the interpretations of the results consistent with design and analysis?
- Are the results consistent with findings from similar studies?
- What do the results mean to medicine and health care, to health care workers and patients?
- Can the results be applied to your practice or research?

Secondary source

- In science, technology, and medicine[edit]
- In general, secondary sources are self-described as review articles or meta-analysis.
- Primary source materials are typically defined as "original research papers written by the scientists who actually conducted the study." An example of primary source material is the Purpose, Methods, Results, Conclusions sections of a research paper (in IMRAD style) in a scientific journal by the authors who conducted the study.[14] In some fields, a secondary source materials may include a summary of the literature in the Introduction of a scientific paper, a description of what is known about a disease or treatment in a chapter in a reference book, or a synthesis written to review available literature.[14] A survey of previous work in the field in a primary peer-reviewed source is secondary source information. This allows secondary sourcing of recent findings in areas where full review articles have not yet been published.

How to Determine the Validity of a Research Article

Open access publishing, article downloads, and citations: randomised controlled trial

- Open access publishing may reach more readers than subscription access publishing. No evidence was found of a citation advantage for open access articles in the first year after publication. The citation advantage from open access reported widely in the literature may be an artefact of other causes.

- What Kinds of Information Do You Need?
- Do you need books? Articles? Newspapers? Statistics?
- Have you been asked to use primary sources? *Primary sources* are documents or other original sources created at the time of an event, and include official records, correspondence, memoirs, diaries, speeches, newspaper articles, photographs and more. *Secondary sources* synthesize the information provided by primary sources and include interpretations, criticisms, evaluations, and summaries. Textbooks, edited books, biographies and review articles are examples of secondary sources

There are different types of academic/scholarly articles

- Original articles consist of study reports and describe results obtained from research for the first time
- Review articles are critical evaluations of studies that have already been published
- Theoretical articles are reports in which the authors are trying to formulate new theories based on existing research

How to Find the Best Sources to Cite for an Academic Paper

- Use Internet sources carefully and sparingly. Let them guide you towards more traditional sources of information.

  Read academic articles on the subject you are writing about. Try to stick to articles from peer-reviewed journals.
- When you find an article you like, look at the bibliography. Repeat this step as often as possible. Look for books and articles mentioned in multiple bibliographies. These are likely some of the most widely regarded articles on the topic.
- Find, read and cite the articles that are mentioned regularly in other articles.
-