THE CLINICAL ACADEMIA

VOLUME **41** ISSUE **2**
MARCH-APRIL 2017

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WWW.THECLINICALACADEMIA.ORG

PRINTED IN THE USA
ISSN: 2465-4027


I don't want you to be only
a doctor but I also want you
to be a man
A quotation by His Royal Highness Prince Mahidol of Songkla

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Our journal is an opened access international journal devoted to peer-reviewed contributions dealing with clinical medicine and medical education from experimental to clinical aspects. Our journal publishes only high quality research, review and other types of original articles, technical and clinical reports every two months. Reviews of various global and Asian aspects will be solicited. Innovation or epidemiological aspects as well as health system research will be addressed. Rigorous systematic review and neglected tropical diseases are our priority

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FORMER

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message from the editor

Hello readers! I hope this message finds you well. This is the second issue of this year. For this issue, there are three original articles and one systematic review from the authors who all used to be the medical students at Khon Kaen Medical Education Center, Khon Kaen Hospital. All of their research are the result of the research-based curriculum. Thailand is now moving towards Thailand 4.0. The research-based curriculum is what we also called Education 4.0 as well. I do hope that our readers would enjoy reading our journal as much as I do.

Thammasorn Jeeeraaumponwat, M.D., Ph.D.
Editor-in-Chief of The Clinical Academia

submission

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Our issues of each volume will be published online
on
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reviewing process

All accepted articles are classified into two main categories;
"***standard submission***" with the approximated processing time of 3-4 months and "***expression submission***" with the approximated processing time of 1-2 months. For the latter category, the author must submit as standard submission with notifying our journal for express submission.

Email: theclinicalacademia@gmail.com
Telephone: (+66) 095 356 2522
Official LINE: @thaimaf

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International Committee of Medical Journal Editors (ICMJE)

Recommendation for Preparing for Submission

1. General Principles

The text of articles reporting original research is usually divided into Introduction, Methods, Results, and Discussion sections. This so-called "IMRAD" structure is not an arbitrary publication format but a reflection of the process of scientific discovery. Articles often need subheadings within these sections to further organize their content. Other types of articles, such as meta-analyses, may require different formats, while case reports, narrative reviews, and editorials may have less structured or unstructured formats.

Electronic formats have created opportunities for adding details or sections, layering information, cross-linking, or extracting portions of articles in electronic versions. Supplementary electronic-only material should be submitted and sent for peer review simultaneously with the primary manuscript.

2. Reporting Guidelines

Reporting guidelines have been developed for different study designs; examples include CONSORT for randomized trials, STROBE for observational studies, PRISMA for systematic reviews and meta-analyses, and STARD for studies of diagnostic accuracy. Journals are encouraged to ask authors to follow these guidelines because they help authors describe the study in enough detail for it to be evaluated by editors, reviewers, readers, and other researchers evaluating the medical literature. Authors of review manuscripts are encouraged to describe the methods used for locating, select¬ing, extracting, and synthesizing data; this is mandatory for systematic reviews. Good sources for reporting guidelines are the EQUATOR Network and the NLM's Research Reporting Guidelines and Initiatives.

3. Manuscript Sections

The following are general requirements for reporting within sections of all study designs and manuscript formats.

a. Title Page

General information about an article and its authors is presented on a manuscript title page and usually includes the article title, author information, any disclaimers, sources of support, word count, and sometimes the number of tables and figures.

Article title. The title provides a distilled description of the complete article and should include information that, along with the Abstract, will make electronic retrieval of the article sensitive and specific. Reporting guidelines recommend and some journals require that information about the study design be a part of the title (particularly important for randomized trials and systematic reviews and meta-analyses). Some journals require a short title, usually no more than 40 characters (including letters and spaces) on the title page or as a separate entry in an electronic submission system. Electronic submission systems may restrict the number of characters in the title.
Author information: Each author's highest academic degrees should be listed, although some journals do not publish these. The name of the department(s) and institution(s) or organizations where the work should be attributed should be specified. Most electronic submission systems require that authors provide full contact information, including land mail and e-mail addresses, but the title page should list the corresponding authors' telephone and fax numbers and e-mail address. ICMJE encourages the listing of authors' Open Researcher and Contributor Identification (ORCID).

Disclaimers. An example of a disclaimer is an author's statement that the views expressed in the submitted article are his or her own and not an official position of the institution or funder.

Source(s) of support. These include grants, equipment, drugs, and/or other support that facilitated conduct of the work described in the article or the writing of the article itself.

Word count. A word count for the paper's text, excluding its abstract, acknowledgments, tables, figure legends, and references, allows editors and reviewers to assess whether the information contained in the paper warrants the paper's length, and whether the submitted manuscript fits within the journal's formats and word limits. A separate word count for the Abstract is useful for the same reason.

Number of figures and tables. Some submission systems require specification of the number of Figures and Tables before uploading the relevant files. These numbers allow editorial staff and reviewers to confirm that all figures and tables were actually included with the manuscript and, because Tables and Figures occupy space, to assess if the information provided by the figures and tables warrants the paper's length and if the manuscript fits within the journal's space limits.

Conflict of Interest declaration. Conflict of interest information for each author needs to be part of the manuscript; each journal should develop standards with regard to the form the information should take and where it will be posted. The ICMJE has developed a uniform conflict of interest disclosure form for use by ICMJE member journals and the ICMJE encourages other journals to adopt it. Despite availability of the form, editors may require conflict of interest declarations on the manuscript title page to save the work of collecting forms from each author prior to making an editorial decision or to save reviewers and readers the work of reading each author's form.

b. Abstract

Original research, systematic reviews, and meta-analyses require structured abstracts. The abstract should provide the context or background for the study and should state the study's purpose, basic procedures (selection of study participants, settings, measurements, analytical methods), main findings (giving specific effect sizes and their statistical and clinical significance, if possible), and principal conclusions. It should emphasize new and important aspects of the study or observations, note important limitations, and not over-interpret findings. Clinical trial abstracts should include items that the CONSORT group has identified as essential. Funding sources should be listed separately after the Abstract to facilitate proper display and indexing for search retrieval by MEDLINE.

Because abstracts are the only substantive portion of the article indexed in many electronic databases, and the only portion many readers read, authors need to ensure that they accurately reflect the content of the article. Unfortunately, information in abstracts often differs from that in the text. Authors and editors should work in the process of revision and review to ensure that information is consistent in both places. The format required for structured abstracts differs from journal to journal, and some journals use more than one format; authors need to prepare their abstracts in the format specified by the journal they have chosen.

The ICMJE recommends that journals publish the clinical trial registration number at the end of the abstract. The ICMJE also recommends that, when a

registration number is available, authors list that number the first time they use a trial acronym to refer to the trial they are reporting or to other trials that they mention in the manuscript. If the data have been deposited in a public repository, authors should state at the end of the abstract the data set name, repository name and number.

c. Introduction

Provide a context or background for the study (that is, the nature of the problem and its significance). State the specific purpose or research objective of, or hypothesis tested by, the study or observation. Cite only directly pertinent references, and do not include data or conclusions from the work being reported.

d. Methods

The guiding principle of the Methods section should be clarity about how and why a study was done in a particular way. Methods section should aim to be sufficiently detailed such that others with access to the data would be able to reproduce the results. In general, the section should include only information that was available at the time the plan or protocol for the study was being written; all information obtained during the study belongs in the Results section. If an organization was paid or otherwise contracted to help conduct the research (examples include data collection and management), then this should be detailed in the methods.

The Methods section should include a statement indicating that the research was approved or exempted from the need for review by the responsible review committee (institutional or national). If no formal ethics committee is available, a statement indicating that the research was conducted according to the principles of the Declaration of Helsinki should be included.

i. Selection and Description of Participants

Clearly describe the selection of observational or experimental participants (healthy individuals or patients, including controls), including eligibility and exclusion criteria and a description of the source population. Because the relevance of such variables as age, sex, or ethnicity is not always known at the time of study design, researchers should aim for inclusion of representative populations into all study types and at a minimum provide descriptive data for these and other relevant demographic variables. If the study was done involving an exclusive population, for example in only one sex, authors should justify why, except in obvious cases (e.g., prostate cancer)." Authors should define how they measured race or ethnicity and justify their relevance.

ii. Technical Information

Specify the study's main and secondary objectives–usually identified as primary and secondary outcomes. Identify methods, equipment (give the manufacturer's name and address in parentheses), and procedures in sufficient detail to allow others to reproduce the results. Give references to established methods, including statistical methods (see below); provide references and brief descriptions for methods that have been published but are not well-known; describe new or substantially modified methods, give the reasons for using them, and evaluate their limitations. Identify precisely all drugs and chemicals used, including generic name(s), dose(s), and route(s) of administration. Identify appropriate scientific names and gene names.

iii. Statistics

Describe statistical methods with enough detail to enable a knowledgeable reader with access to the original data to judge its appropriateness for the study and to verify the reported results. When possible, quantify findings and present them with appropriate indicators of measurement error or uncertainty (such as confidence intervals). Avoid relying solely on statistical hypothesis testing, such as P values, which fail to convey important information about effect size and precision of estimates. References for the design of the study and statistical methods should be to standard works when possible (with pages stated). Define statistical terms, abbreviations, and most symbols. Specify the statistical software package(s) and versions used. Distinguish prespecified from exploratory analyses, including subgroup analyses.

e. Results

Present your results in logical sequence in the text, tables, and figures, giving the main or most important findings first. Do not repeat all the data in the tables or figures in the text; emphasize or summarize only the most important observations. Provide data on all primary and secondary outcomes identified in the Methods Section. Extra or supplementary materials and technical details can be placed in an appendix where they will be accessible but will not interrupt the flow of the text, or they can be published solely in the electronic version of the journal.

Give numeric results not only as derivatives (for example, percentages) but also as the absolute numbers from which the derivatives were calculated, and specify the statistical significance attached to them, if any. Restrict tables and figures to those needed to explain the argument of the paper and to assess supporting data. Use graphs as an alternative to tables with many entries; do not duplicate data in graphs and tables. Avoid nontechnical uses of technical terms in statistics, such as "random" (which implies a randomizing device), "normal," "significant," "correlations," and "sample."

Separate reporting of data by demographic variables, such as age and sex, facilitate pooling of data for subgroups across studies and should be routine, unless there are compelling reasons not to stratify reporting, which should be explained.

f. Discussion

It is useful to begin the discussion by briefly summarizing the main findings, and explore possible mechanisms or explanations for these findings. Emphasize the new and important aspects of your study and put your finings in the context of the totality of the relevant evidence. State the limitations of your study, and explore the implications of your findings for future research and for clinical practice or policy. Do not repeat in detail data or other information given in other parts of the manuscript, such as in the Introduction or the Results section.

Link the conclusions with the goals of the study but avoid unqualified statements and conclusions not adequately supported by the data. In particular, distinguish between clinical and statistical significance, and avoid making statements on economic benefits and costs unless the manuscript includes the appropriate economic data and analyses. Avoid claiming priority or alluding to work that has not been completed. State new hypotheses when warranted, but label them clearly.

g. References

i. General Considerations Related to References

Authors should provide direct references to original research sources whenever possible. References should not be used by authors, editors, or peer reviewers to promote self-interests.Although references to review articles can be an efficient way to guide readers to a body of literature, review articles do not always reflect original work accurately. On the other hand, extensive lists of references to original work on a topic can use excessive space. Fewer references to key original papers often serve as well as more exhaustive lists, particularly since references can now be added to the electronic version of published papers, and since electronic literature searching allows readers to retrieve published literature efficiently.

Do not use conference abstracts as references: they can be cited in the text, in parentheses, but not as page footnotes. References to papers accepted but not yet published should be designated as "in press" or "forthcoming." Information from manuscripts submitted but not accepted should be cited in the text as "unpublished observations" with written permission from the source.

Avoid citing a "personal communication" unless it provides essential information not available from a public source, in which case the name of the person and date of communication should be cited in parentheses in the text. For scientific articles, obtain written permission and confirmation of accuracy from the source of a personal communication.

Some but not all journals check the accuracy of all reference citations; thus, citation errors sometimes appear in the published version of articles. To minimize such errors, references should be verified using either an electronic bibliographic source, such as PubMed, or print copies from original sources. Authors are responsible for checking that none of the references cite retracted articles except in the context of referring to the retraction. For articles published in journals indexed in MEDLINE, the ICMJE considers PubMed the authoritative source for information about retractions. Authors can identify retracted articles in MEDLINE by searching PubMed for "Retracted publication [pt]", where the term "pt" in square brackets stands for publication type, or by going directly to the PubMed's list of retracted publications.

References should be numbered consecutively in the order in which they are first mentioned in the text. Identify references in text, tables, and legends by Arabic numerals in parentheses.

References cited only in tables or figure legends should be numbered in accordance with the sequence established by the first identification in the text of the particular table or figure. The titles of journals should be abbreviated according to the style used for MEDLINE (www.ncbi.nlm.nih.gov/nlmcatalog/journals). Journals vary on whether they ask authors to cite electronic references within parentheses in the text or in numbered references following the text. Authors should consult with the journal to which they plan to submit their work.

ii. Reference Style and Format

References should follow the standards summarized in the NLM's International Committee of Medical Journal Editors (ICMJE) Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals: Sample References webpage and detailed in the

NLM's Citing Medicine, 2nd edition. These resources are regularly updated as new media develop, and currently include guidance for print documents; unpublished material; audio and visual media; material on CD-ROM, DVD, or disk; and material on the Internet.

h. Tables

Tables capture information concisely and display it efficiently; they also provide information at any desired level of detail and precision. Including data in tables rather than text frequently makes it possible to reduce the length of the text.

Prepare tables according to the specific journal's requirements; to avoid errors it is best if tables can be directly imported into the journal's publication software. Number tables consecutively in the order of their first citation in the text and supply a title for each. Titles in tables should be short but self-explanatory, containing information that allows readers to understand the table's content without having to go back to the text. Be sure that each table is cited in the text.

Give each column a short or an abbreviated heading. Authors should place explanatory matter in footnotes, not in the heading. Explain all nonstandard abbreviations in footnotes, and use symbols to explain information if needed. Symbols may vary from journal to journal (alphabet letter or such symbols as *, †, ‡, §), so check each journal's instructions for authors for required practice. Identify statistical measures of variations, such as standard deviation and standard error of the mean.

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Additional tables containing backup data too extensive to publish in print may be appropriate for publication in the electronic version of the journal, deposited with an archival service, or made available to readers directly by the authors. An appropriate statement should be added to the text to inform readers that this additional information is available and where it is located. Submit such tables for consideration with the paper so that they will be available to the peer reviewers.

i. Illustrations (Figures)

Digital images of manuscript illustrations should be submitted in a suitable format for print publication. Most submission systems have detailed instructions on the quality of images and check them after manuscript upload. For print submissions, figures should be either professionally drawn and photographed, or submitted as photographic-quality digital prints.

For X-ray films, scans, and other diagnostic images, as well as pictures of pathology specimens or photomicrographs, send high-resolution photographic image files. Since blots are used as primary evidence in many scientific articles, editors may require deposition of the original photographs of blots on the journal's website.

Although some journals redraw figures, many do not. Letters, numbers, and symbols on figures should therefore be clear and consistent throughout, and large enough to remain legible when the figure is reduced for publication. Figures should be made as self-explanatory as possible, since many will be used directly in slide presentations. Titles and detailed explanations belong in the legends—not on the illustrations themselves.

Photomicrographs should have internal scale markers. Symbols, arrows, or letters used in photomicrographs should contrast with the background. Explain the internal scale and identify the method of staining in photomicrographs.

Figures should be numbered consecutively according to the order in which they have been cited in the text. If a figure has been published previously, acknowledge the original source and submit written permission from the copyright holder to reproduce it. Permission is required irrespective of authorship or publisher except for documents in the public domain.

In the manuscript, legends for illustrations should be on a separate page, with Arabic numerals corresponding to the illustrations. When symbols, arrows, numbers, or letters are used to identify parts of the illustrations, identify and explain each one clearly in the legend.

j. Units of Measurement

Measurements of length, height, weight, and volume should be reported in metric units (meter, kilogram, or liter) or their decimal multiples.

Temperatures should be in degrees Celsius. Blood pressures should be in millimeters of mercury, unless other units are specifically required by the journal.

Journals vary in the units they use for reporting hematologic, clinical chemistry, and other measurements. Authors must consult the Information for Authors of the particular journal and should report laboratory information in both local and International System of Units (SI).

Editors may request that authors add alternative or non-SI units, since SI units are not universally used. Drug concentrations may be reported in either SI or mass units, but the alternative should be provided in parentheses where appropriate.

k. Abbreviations and Symbols

Use only standard abbreviations; use of nonstandard abbreviations can be confusing to readers. Avoid abbreviations in the title of the manuscript. The spelled-out abbreviation followed by the abbreviation in parenthesis should be used on first mention unless the abbreviation is a standard unit of measurement.

Time of self-harm and risk for death: 20-year retrospective cohort study

ORIGINAL ARTICLE BY

Sirina Satthapisit[1], M.D., Nithikorn Sorncha[2], M.D.

[1]Department of Psychiatry, Khon Kaen Hospital, Thailand, [2]Department of Social Medicine, Khon Kaen Hospital, Thailand

Accepted: December 2016
Latest revision: February 2017
Printed: April 2017

Correspondence to: Sirina Satthapisit; s.satthapisit@gmail.com

ABSTRACT

OBJECTIVE

To determine the association between time of self-harm and risk for death.

METHODS

This is a retrospective cohort study using 20-year, 1997 to 2016, database of Khon Kaen Hospital Trauma Registry of all patients who visit with self-harm at the emergency department. The risk factor of interest was the time of self-harm which was divided into eight periods. The primary outcome of the study was death.

RESULTS

There were 6,022 patients with self-harm during the study period with 239 deaths. Time of self-harm was not found to be associated with death. However, factors found to be associated with higher death rate were male sex (adjusted odds ratio (AOR), 1.98; 95% confidence interval (CI), 1.43 to 2.75), hanging (AOR, 21.08; 95% CI, 14.35 to 30.97), ingesting pesticide (AOR, 6.62: 95% CI, 4.61 to 9.50) and using firearm (AOR, 18.51; 95% CI 9.70 to 35.31) as methods of self-harm. The peak time of self-harm was evening period (18:01 to 21:00). Case fatality rate was 4% and their most common method was ingesting pesticide.

CONCLUSION

There was no association between the time of self-harm and death. Factors found to be associated with higher death rate were male sex, hanging, ingesting pesticide and using firearm.

INTRODUCTION

Estimated annual death rate of self-harm is 11.4 deaths per 100,000 globally.[1] In Thailand, the rate of self-harm was approximately 7.3 per 100,000 in 2015.[2] Even with no death, self-harm still one of the major cause of economic burden due to a high volume of health care utilization.[3] Naturally occurring alternation of light and dark is one of the risks for self-harm[4] as photoperiod variations lead to subsequent changes of mood and impulsivity induced by the serotonergic pathway.[5] However, from previous studies, their findings still controversial regarding the most common time of self-harm, for instance, morning time was reported to be common for self-harm in the elderly[4,6,7] while the late evening was also reported to be the most common time for self-harm.[8] Moreover, the self-harm in female tends to be earlier of the day.[9,10]

The incidence, trends, and patterns of self-harm differ considerably between Asian and Western countries.[11] In general, seasons are less to affect suicide due to the narrow gradients with no extreme weather condition as well as the problem regarding daylight is also not an issue in most of the tropical countries.[12]

Furthermore, few studies have examined the timing of self-harm and the risk of death that their findings are also still controversial; a study from Sri Lanka found that self-harm in the evening was associated with higher mortality rate.[13] However, two Italian studies found that the self-harm between 6:00 and 16:00 was associated with higher mortality rate.[4,14] Moreover, the conclusion of these studies was solely based on the assumed fatal self-harm times from death certificate.[4,14] Thus, the aim of this study was to determine the possible association between the time of self-harm and risk of death.

METHODS

STUDY DESIGN

This is a retrospective cohort study by reviewing and verifying 20-year medical records of patients diagnosed with self-harm visiting Khon Kaen Hospital between 1997 and 2016 to identify the association between the time of self-harm and death.

ETHICAL CONSIDERATION

The protocol of the present study was reviewed and approved by Institutional Review Board of Khon Kaen Hospital (approval number: KE59116). It followed the principles of the Declaration of Helsinki, October 2013.

EXPOSURES

Exposure of our interest was the time of self-harm which was identified by interviewing the patient or relative or courier in the unconscious case for precise estimation rather than time assuming. It was divided into eight periods starting from 0.01 to 3.00 am and so on.

OUTCOMES

The outcome of the study was overall death including death before arrival, death at the emergency department, and death after

Table 1. Characteristics of the patients

Characteristic	0:01-3:00 (n=554)	3:01-6:00 (n=328)	6:01-9:00 (n=519)	9:01-12:00 (n=695)	12:01-15:00 (n=693)	15:01-18:00 (n=950)	18:01-21:00 (n=1,364)	21:01-24:00 (n=929)	P value
Age-yr									0.005
10 or younger	0	0	1 (0.2)	3 (0.4)	2 (0.3)	6 (0.6)	3 (0.2)	2 (0.2)	
11-19	149 (27.4)	7 (22.3)	112 (21.6)	156 (22.4)	148 (21.4)	245 (25.8)	377 (27.6)	276 (29.7)	
20-35	324 (59.6)	194 (59.1)	266 (51.3)	346 (49.8)	383 (55.3)	480 (50.5)	695 (51.0)	509 (54.8)	
36-45	54 (9.9)	28 (8.5)	81 (15.6)	119 (17.1)	90 (13.0)	139 (14.6)	187 (13.7)	104 (11.2)	
46-60	14 (2.6)	23 (7.0)	23 (7.0)	54 (7.8)	57 (8.2)	66 (6.9)	83 (6.1)	33 (3.6)	
Older than 60	3 (0.6)	10 (3.0)	17 (3.3)	17 (2.4)	13 (1.9)	14 (1.5)	19 (1.4)	5 (0.5)	
Male sex-no. (%)	259 (47.6)	147 (44.8)	221 (42.6)	312 (44.9)	351 (50.6)	504 (53.1)	699 (51.2)	433 (46.6)	0.01
Self-harm at home-no. (%)	227 (41.7)	140 (42.7)	256 (49.3)	319 (45.9)	333 (48.1)	423 (44.5)	648 (47.5)	415 (44.7)	0.31
Alcohol use-no. (%)	15 (57.7)	7 (63.6)	7 (23.3)	5 (18.5)	4 (14.3)	8 (27.6)	20 (43.5)	9 (16.1)	0.009
Repeated self-harm-no. (%)	34 (6.2)	25 (7.6)	25 (4.8)	34 (4.9)	44 (6.3)	59 (6.2)	91 (6.7)	61 (6.6)	0.43
Methods of self-harm-no. (%)									0.12
Chemical and drug abuse	302 (55.5)	188 (57.3)	329 (75.5)	524 (75.4)	509 (72.4)	671 (69.6)	970 (63.8)	539 (63.8)	
Hanging	15 (2.8)	16 (4.9)	29 (5.6)	33 (4.7)	41 (5.9)	55 (5.8)	71 (5.21)	29 (3.1)	
Sharp object	156 (28.7)	88 (26.8)	61 (11.8)	95 (13.7)	100 (14.4)	177 (18.6)	302 (22.1)	220 (23.7)	
Blunt object	30 (5.5)	13 (4.0)	14 (2.7)	16 (2.3)	26 (3.8)	31 (3.3)	73 (5.4)	44 (4.7)	
Other	41 (7.5)	23 (7.0)	23 (4.4)	27 (3.9)	24 (3.5)	26 (2.7)	48 (3.5)	43 (4.6)	

admission. Other outcomes were denial to treatment, refer to other hospitals and discharge after full recovery.

DATA COLLECTION

The present study used the data from trauma registry which was established in 1989. The registry contained data regarding patients with self-harm[15] according to the International Classification of Disease, 10th revision (ICD-10) with the category of intentional self-harm (X60-X84).[16] From the registry, we extracted data regarding age, sex, place, alcohol use, repeated self-harm, methods, time of self-harm and outcomes of the treatment.

STATISTICAL ANALYSIS

Frequency table was generated for each variable to identify the wide values. All data were cleaned before analysis. For descriptive statistics, number and percentage were used to summarize categorical variables while mean together with standard deviation (SD) were used to summarized normally distributed continuous data and median together with interquartile range (IQR) were used to summarize non-normally distributed

Table 2. Treatment outcomes

Outcome	0:01-3:00 (n=554)	3:01-6:00 (n=328)	6:01-9:00 (n=519)	9:01-12:00 (n=695)	12:01-15:00 (n=693)	15:01-18:00 (n=950)	18:01-21:00 (n=1,364)	21:01-24:00 (n=929)	Total
					no. (%)				
Death before arrival	0	0	0	1 (0.1)	0	1 (0.1)	1 (0.1)	1 (0.1)	4 (0.1)
Death at the emergency room	1 (0.2)	2 (0.6)	2 (0.4)	5 (0.7)	4 (0.6)	4 (0.4)	7 (0.5)	2 (0.2)	27 (0.4)
Discharge home	198 (36.4)	100 (30.6)	80 (15.4)	98 (14.2)	102 (14.7)	144 (15.2)	274 (20.2)	251 (27.1)	1,247 (20.7)
Refer to other hospitals	6 (1.1)	4 (1.2)	5 (1.0)	8 (1.2)	7 (1.0)	5 (0.5)	6 (0.4)	7 (0.8)	48 (0.8)
Denial treatment at the emergency room	26 (4.8)	11 (3.4)	5 (1.0)	12 (1.7)	10 (1.5)	7 (0.7)	16 (1.2)	11 (1.2)	147 (2.4)
Admission	313 (57.5)	210 (64.2)	427 (82.3)	568 (82.1)	656 (81.5)	726 (81.7)	1,039 (76.5)	610 (69.0)	4,627 (87.6)
Discharge home	269 (88.8)	173 (84.0)	356 (85.0)	468 (85.7)	477 (85.9)	673 (87.6)	996 (88.2)	642 (88.9)	4,054 (87.6)
Refer to other hospitals	12 (4.0)	7 (3.4)	20 (4.8)	34 (6.1)	20 (3.6)	28 (3.7)	39 (3.8)	24 (3.8)	184 (4.0)
Denial treatment after admission	10 (3.3)	9 (4.3)	19 (4.6)	20 (3.6)	27 (4.9)	26 (3.4)	46 (4.5)	24 (3.7)	181 (3.9)
Death after admission	12 (4.0)	17 (8.3)	24 (5.7)	26 (4.7)	31 (5.6)	41 (5.4)	35 (3.4)	22 (3.5)	208 (4.5)

continuous data. Logistic regression was used to identify factors predicting death from self-harm, adjusted odds ratio (AOR) was presented together with its 95% confidence interval (CI).

RESULTS

PATIENTS' CHARACTERISTICS

From our 20-years database, there were 433,752 patients with injuries visiting the emergency department of Khon Kaen Hospital. Of these, there were 6,022 (1.3%) patients with self-harm, averagely 2 cases a day.

The peak time of self-harm was evening period (18:01 to 21:00) (1,364 patients, 22.7%). Their mean age was 27.8±11.3 years. Almost all of them were early adults. A bit more than half were female. Of 6,022, 45.8% did self-harm in their homes. Only 75 patients (1.2%) stated that they drank alcohol. Repeated self-harm was found in 373 patients (6.1%).

Age, male sex, and alcohol use were found to be associated with eight periods of time of self-harm; the proportion of patients aged 60 years or older was highest during 6:01 to 9:00 (P=0.005), the proportion of male patients was highest during 15:01 to 18:00 (P=0.01), and the proportion of patient who used alcohol was highest during 3:01 to 6:00 (P=0.009) (Table 1).

METHODS OF SELF-HARM

Of 6,022, chemical and drug abuse was the most common method throughout the day, accounting for a total of 4,032 patients (Table 1).The second-most common method of self-harm was using sharp objects (1,199 patients, 19.9%) following by self-harm by hanging 289 (4.8%), jumping from

Table 3. Factors predicting all-cause mortality

Factor	Adjusted odds ratio (95% confidence interval)
Male sex	1.98 (1.43-2.75)
Age-yr	1.04 (1.03-1.05)
Time of self harm	
0:01-3:00	Reference
3:01-6:00	1.25 (0.56-2.77)
6:01-9:00	1.01 (0.49-2.10)
9:01-12.00	0.91 (0.45-1.84)
12:01-15:00	0.94 (0.47-1.90)
15:01-18:00	1.07 (0.55-2.10)
18:01-21:00	0.70 (0.36-1.39)
21:01-24.00	0.86 (0.42-1.76)
Hanging	21.08 (14.35-30.97)
Ingesting pesticide	6.62 (4.61-9.50)
Using firearm	18.51 (9.70-35.31)
Making self drown	7.17 (0.89-57.51)

the height 82 (1.4%), using firearm 66 (1.1%), and making self-drown 13 (0.2%).

TREATMENT OUTCOME

Of 6,022 arriving at emergency department, 1,247 (20.7%) were home discharged. Most of them were hospitalized (4,627 patients, 76.8%), 147 (2.4%) of the patients with self-harm were denial all treatment. Forty-eight (0.8%) referred to other hospitals according to insurance status and their requirement. After admission of 4,627 patients, majority of them (4,054 patients, 87.6%) were clinically improved and were later home discharged, 184 (4.1%) were referred to other hospitals after admission especially the mental hospital, 181 patients (4.0%) were denied all treatment after admission (Table 2).

In total, 239 were dead from self-harm with case fatality rate of 4%. Rates of death were similar throughout the day. Of these, 4 (1.7%) died before arriving the hospital, 27 (11.3%) died at the emergency department and 208 (87.0%) died after admission. The majority of those who died were male (76.6%). Ingesting pesticide (36.8%), acetaminophen (1.3%), and other chemicals (12.2%) were the leading cause of death following by hanging (32.2%), using firearm (6.7%), jumping from the height (4.2%), using explosive (2.9%), using sharp object (2.9%), using blunt object (0.4%) and making self-drown

(0.4%). Of 239, the most common period of fatal self-harm was 15:01 to 18:00 (19.2%), followed by 18:01 to 21:00 (18.0%), and the most common age group of fatal self harm was 20 to 35 years old.

TIME OF SELF-HARM AND RISK OF DEATH

From logistic regression, we found no association between the clock time defined into eight periods of self-harm and risk for death. However, factors found to be associated with higher death rate were male sex (AOR, 1.98; 95% CI, 1.43 to 2.75), hanging (AOR, 21.08: 95% CI, 14.35 to 30.97), ingesting pesticide (AOR, 6.62: 95% CI, 4.61 to 9.50) and using firearm (AOR, 18.51; 95% CI, 9.70 to 35.31) (Table 3).

DISCUSSION

MAJOR FINDINGS

In this study, there was no association between the time of self-harm and risk for death. However, the factors found to be associated with higher death rate were male sex, hanging, ingesting pesticide and using firearm. The peak time of self-harm was evening period (18:01 to 21:00). Case fatality rate was 4% and their most common method was ingesting pesticide.

COMPARISON WITH OTHER STUDIES

Self-harm is a complex issue caused by multifactorial factors.[17] Previous studies have examined the time of self-harm, however, there have been no consistent results.[4,14,14] Moreover, evidence of the time of self-harm and risk for death is still scarce. Our study suggested that time of self-harm was not associated with death. This was similar to a previous study, that found time of self-poisoning with ingesting pesticide including carbamate, organophosphate, paraquat, and glyphosate were not related with death[14] even though the circadian clock influences a large number of rhythms in behavior of human being.[18]

In our study, the factors found to be associated with higher death rate were male sex, hanging, ingesting pesticide and using firearm. These were similar to that of previous studies which stated that fatal self-harm was associated with male sex[19] and violent methods such as hanging, making self-drown, using firearm and jumping from the height.[20–26] However, there are some differences among studies, for instance, it found that ingesting pesticide was the most common method used for fatal self-harm in studies from China.[22–24] By contrast, studies from England and Wales and Australia stated that hanging was the most common method used for fatal self-harm,[22] while using firearm was the most common methods of fatal self-harm found in studies from the USA.[25,26] This differences might be due to the favored methods for different population subgroup, age-specific rates for hanging declined aged 30 years while the rates for firearm cases rose with age.[27]

From our study, fatal self-harm was common in early adult (20-35 years old), this was different to the findings from the previous study from the USA which stated that fatal self-harm was common in elderly age group (more than 60 years old).[25,26] This variation might be due case fatality variation between age groups is significant related with methods of fatal self-harm.[27]

Our study found that self-harm was more common in women while fatal self-harm was more common in men. Our findings were supported by the report of World Health Organization which stated that in low- and middle-income countries, ratio male to female for fatal self-harm is about 1.5:1.[1] Our study found that the peak time of self-harm was evening period (18:01 to 21:00), similar to that of the previous study from Sri-Lanka, a country in tropical area. The previous study from Italy stated that the peak time of self-harm was in the late morning (08:00 to 11:00).[5] While the study from Germany, stated that the peak times were in the morning (9:00 to 12:00) and in the evening (18:00 to 21:00).[28] Time variation of fatal self-harm among countries might be from the differences of weather.[12] One of the predictors for fatal self-harm is the history of previous self-harm.[24,29] In our study, the 20-year record was found only 6.2% of patients with repeated self-harm. However, we were unable to identify the association between repeated self-harm and death due to the validity of the information. Alcohol and other substance use were found relatively high in those with self-harm.[29,30] One fifth of committed suicide was associated with alcohol.[31] But our study found the patient accepted of drinking alcohol was only 1.2%. This might be due to the fact that patient might avoid talking about their alcohol consumption.

STRENGTH AND LIMITATIONS

This was the first study, to our knowledge, exhibit the relationship between time of self-harm and death that using time of self-harm from the report of the patients themselves or their relatives or couriers rather than from death certificate. The closest possible time for self-harm was then well estimated.

However, there were several limitations of our study. Firstly, our study was a retrospective in nature, data completeness was still varied. For instance, history of underlying diseases was not all included in the database. Thus, we were unable to evaluate whether patients' illness such as their psychiatric and medical conditions were the risk their death. Secondly, our study unable to evaluate the previous self-harm as no primary data were retrieved from the database. Repeated self-harm in the present study was solely from the manual counting of those appeared more than once in the database in the 20-year period of the database. Thirdly, alcohol intake was recorded regardless of the quantity of alcohol consumption. Hence, the association between alcohol consumption and death could not be precisely estimated.

CONCLUSION AND IMPLICATION

There was no association between the time of self-harm and death. The peak time of self-harm was evening period (18:01 to 21:00). In our study, factors found to be associated with higher death rate were male sex, hanging, ingesting pesticide and using firearm. For better understanding of the relationship between time of self-harm and risk for death in those with self-harm, a larger prospective multi-center cohort study should be conducted in the future.

ACKNOWLEDGMENTS & DECLARATION

We would like to thank Dr. Witaya Chadbunchachai, Ms. VarunchapornPolkert, Trauma Registry Team and Department of Psychiatry, Khon Kaen Hospital for the data contribution. We also would like to thank Dr. Thammasorn Jeeraaumponwat for his suggestions and statistical analysis.

COMPETING INTERESTS: All authors read and approved the final manuscript and agreed to be accountable for all aspects therein. The authors report no conflicts of interest related to this work.

FUNDING: None

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Preeclampsia and infantile birth weight by maternal age group

ORIGINAL ARTICLE BY

Darin Siripiriyakul[1], M.D., Patima Treepong[2,], M.D., Thodsapol Trijitwathanakul[3], M.D.

[1]Kantharawichai Hospital, Thailand; [2]Roi Et Hospital, Thailand; [3]Nongkhai-Wattana Hospital, Thailand.

Accepted: December 2016
Latest revision: March 2017
Printed: April 2017

Correspondence to: Thodsapol Trijitwathanakul; ttrijitwatthanakul@gmail.com

ABSTRACT

OBJECTIVE

To examine the association between preeclampsia and infantile birth weight by maternal age group.

METHODS

We conducted a hospital-based, case-control study using data obtained from the medical records of Khon Kaen Hospital, Thailand. Case patients were eligible for inclusion if they gave birth to live singleton infants at Khon Kaen Hospital from July 2012 through July 2013 and were diagnosed as having preeclampsia. Age and residence-matched controls were selected from women who gave birth at Khon Kaen Hospital during the same period without preeclampsia. Both case and control patients were categorized according to their age; teenage, normal age and elderly. We, later, assessed the associations between maternal age and neonatal birth weight.

RESULTS

The medical records of 320 mothers were screened for identification of the cases, 179 of those with the diagnosis of preeclampsia were included as case patients. With the ratio of 1:2, another 358 control patients were included in this study. In the preeclampsia group, there were no significant differences among the three groups, teenage pregnancy, normal age pregnancy and elderly pregnancy, regarding birth weight (P=0.842) as those without preeclampsia, there were no significant differences among the three groups regarding birth weight (P=0.253). The logistic regression found that gestational age (adjusted odds ratio (AOR), 0.46; 95% confidence interval (CI) 0.38 to 0.56) and body mass index (AOR, 0.88; 95% CI, 0.82 to 0.95) decreased the chance of having low birth weight infants while preeclampsia (AOR, 4.34; 95% CI, 2.18 to 8.64) increased the chance of having low birth weight infants.

CONCLUSION

Age group was not associated with infantile birth weight in both those with and without preeclampsia. However, gestational age and body mass index lower the chance of having low birth weight infants while preeclampsia increased the chance of having low birth weight infants.

INTRODUCTION

Preeclampsia that characterized by new hypertension and proteinuria or superimposed to maternal hypertension or nephropathy in pregnant women who are beyond 20 weeks of gestational age is a leading cause of maternal and infant morbidity and mortality worldwide.[1-3] Moreover, preeclampsia can cause fatal lethal complications including disseminated intravascular coagulation, intracranial hemorrhage, liver and kidney failure, cardiovascular collapse and abnormal uterine and umbilical artery.[4-7] Intrauterine fetal growth restriction (IUGR), intrauterine fetal demise, prematurity, hemolysis, elevated liver enzymes, low platelets (HELLP) syndrome and eclampsia are also related with this obstetric problems.[6-8]

In relation to infantile birth weights, it found that the infants born from mothers with severe preeclampsia were likely to have lower birth weight compared to those with normal pressure, however, in women with mild preeclampsia compared to those with normal pressure, the infantile birth weight tended to be similar.[5] However, there was a study regarding maternal with preeclampsia and infantile birth weight which stated that maternal with preeclampsia was a risk factor for low infantile birth weight.[7] Thus, it is still inconclusive that mothers with preeclampsia are at risk for having low birth weight infants. Moreover, there are no others studies examining the association preeclampsia and infantile birth weight in different maternal age groups. Consequently, we conducted the study to assess the association between preeclampsia and infantile birth weight as well as to identify factors that might influence infantile low birth weight.

METHODS

STUDY DESIGN AND POPULATION

We conducted a hospital-based nested case-control study using data obtained from the medical records from Khon Kaen Hospital, Thailand. Case patients were eligible if they gave birth to live singleton infants in Khon Kaen Hospital from July 2012 through July 2013 and were diagnosed with preeclampsia according to the criteria of the American College of Obstetricians and Gynecologists in 2000.[3] Age and residence-matched controls were selected from women who gave birth at Khon Kaen Hospital during the same period without preeclampsia. Our focus was only preeclampsia, hence, pregnancies complicated by gestational hypertension, pre-eclampsia superimposed on chronic hypertension were excluded. We also excluded those with the following; a pre-pregnancy diagnosis of diabetes, a pre-pregnancy diagnosis of hypertension, gestational diabetes mellitus, fetal death in utero and incomplete data. Later, both case and control patients were categorized according to their age; teenage (less than 20 years), normal age and elderly (more than 35 years).

DEFINITION OF PREECLAMPSIA

We used a definition of preeclampsia by the American College of Obstetricians and

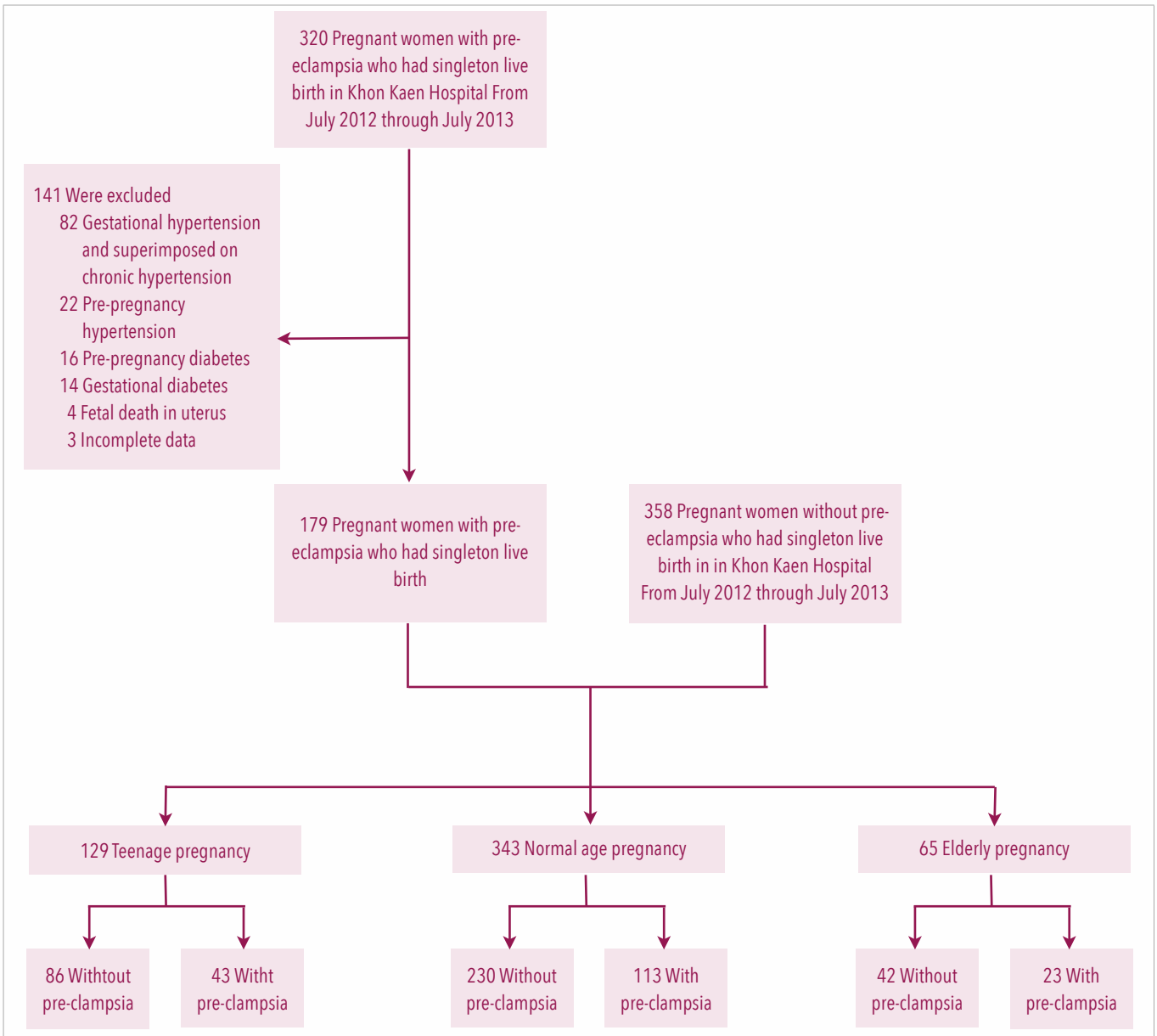

Figure 1. Patient flow chart

Gynecologists in 2000[3] in which persistent diastolic blood pressure of $\geq$90 mmHg has to develop after 20 weeks of the gestation and it has to increase $\geq$ 25 mmHg. Proteinuria also has to be presented with the cutoff 0.3 g/L in 24 hours urine collection (semiquantitative dipstick 1+) in at least one urine sample after 20 weeks of the gestation.

STUDY OUTCOME

The primary outcome of interest was neonatal birth weight and low birth weight equaled to a birth weight lower than 2500 g. The secondary outcome measures included placenta previa, the turbidity of an amniotic fluid, blood loss, APGAR score at 1 minute and 5 minute, perinatal asphyxia, is defined as a failure to start regular respiration within a minute of birth. Diagnosis can be objectively assessed when the APGAR score below 7, and congenital anomalies.

DATA COLLECTION

Demographic variables were derived from medical information from maternal hospitalization data and birth certificates. Maternal variables included age, estimated gestational age, gravidity, parity, height, pre-delivery weight, body mass index, type of delivery, history of smoking and alcohol drinking during pregnancy, underlying diseases such as HIV and syphilis infection, epilepsy, asthma, migraine, viral hepatitis infection, allergic rhinitis, thyroid disease, heart disease and all others as well as variables of the newborn regarding neonatal sex and birth weight.

STATISTICAL ANALYSIS

All data were double entered and cleaned before preceding the analysis. All numeric data were tested for their distribution using Kolmogorov-Smirnov test. Non-normal distributed data were presented using median and interquartile range (IQR) for comparisons the baseline characteristics of the mothers and the newborns. We analyzed characteristics of the mothers that were related to maternal history of preeclampsia in each category using either Pearson's Chi-square or Fisher's exact test where appropriate if there were categorical variables and Mann-Whitney U test or Kruskal-Wallis test if there were scale variables for the comparison between two and three groups, respectively. Risk factor for infantile low birth weight was identified using crude odds ratio (COR) and its 95% confidence intervals (CI). However, to adjust for possible confounders, logistic regression analysis was used to calculate adjusted odds ratio (AOR) and its 95% CI.

RESULTS

PATIENTS

In the present study, the medical records of 320 mothers were screened for identification of the cases, 141 were excluded, 179 of those with the diagnosis of preeclampsia were included as case patients (Figure 1). With the ratio of 1:2, another 358 controls were included in this study. Later, both cases and controls were categorized according to their age group; teenage, normal age and elderly. Their overall median age was 24 year (IQR 20 to 30), median gestational age was 38.6 weeks (IQR 37.7 to 39.4). Most of them were nulliparous with the median height of 158 cm (IQR 155 to 162), the median pre-delivery weight of 68 kg (IQR 60 to 77) and median body mass index of 27.3 kg/m^2 (IQR 24.6 to 30.3).

For those with the diagnosis of preeclampsia, the group of teenage pregnancy had the highest proportion of nulliparous (86.0%; $P<0.001$) and the group of normal age pregnancy

Table 1. Characteristics of the patients

Characteristic	Preeclampsia				No Preeclampsia				P Value*	P Value†	P Value‡	P Value§
	Teenage pregnancy	Normal age pregnancy	Elderly pregnancy	P Value	Teenage pregnancy	Normal age pregnancy	Elderly pregnancy	P Value				
Maternal												
Age-yr				<0.001				<0.001	0.98	0.78	0.72	0.47
Median	18	25	37		17	25	36					
IQR	16-18	22-29	36-40		16-18	22-29	35-38.3					
Gestational age weeks-wk				0.53				0.013	<0.001	0.01	<0.001	0.17
Median	38.3	38	37.7		39	38.9	38					
IQR	36.9-39.3	36.6-39.4	36.0-38.3		38.0-39.6	38.0-39.9	37.4-39.1					
Nulliparous-no. (%)	37 (86.0)	61 (54.0)	6 (26.1)	<0.001	68 (79.1)	90 (39.1)	7 (16.7)	<0.001	0.01	0.34	0.01	0.52
Parity												
Term				<0.001				<0.001	<0.001	0.039	<0.001	0.45
Median	0	0	1		0	1	1					
IQR	0	0-1	0-2		0	0-1	0-2					
Preterm				<0.001				0.002	0.27	1	0.98	0.2
Median	0	0	0		0	0	0					
IQR	0	0-1	0		0	0	0					
Abortion				0.34				0.02	0.24	0.5	0.23	0.86
Median	0	0	0		0	0	0					
IQR	0	0	0		0	0	0-1					
Alive				<0.001				<0.001	0.001	0.04	<0.001	0.92
Median	0	0	1		0	1	1					
IQR	0	0-1	0-2		0	0-1	1-2					
Height-cm				0.14				0.06	0.35	0.13	0.87	0.22
Median	160	158	157		158	158	155					
IQR	156-165	155-161	155-162		155-161	153-162	153-159					
Pre-delivery weight-kg				0.03				0.16	<0.001	0.07	<0.001	0.03
Median	66	75	76.9		64.5	67	67					
IQR	60-78	67-84	62-84		56-72	60-74	60-72.3					
Body mass index-kg/m^2				0.01				0.02	<0.001	0.07	<0.001	0.09
Median	26.7	30.2	28.7		25.1	26.6	27.3					
IQR	24-30	27-33.5	25.8-34.1		23.0-28.1	24.1-29.4	25.2-29.7					

Table 1. (Continued)

Characteristic	Preeclampsia				No Preeclampsia				P Value*	P Value†	P Value‡	P Value§
	Teenage pregnancy	Normal age pregnancy	Elderly pregnancy	P Value	Teenage pregnancy	Normal age pregnancy	Elderly pregnancy	P Value				
Cesarean section-no (%)	19 (44.2)	61 (54.0)	12 (52.2)	0.55	23 (26.7)	96 (41.7)	19 (45.2)	0.03	0.01	0.05	0.03	0.59
Smoking-no (%)	1 (2.3)	1 (0.9)	1 (4.3)	0.307	1 (1.2)	0	0	0.36	0.11	1	0.33	0.35
Alcohol drinking-no (%)	1 (2.3)	1 (0.9)	1 (4.3)	0.31	0	0	0	N/A	0.04	0.33	0.33	0.35
Underlying disease-no (%)												
Anemia	5 (11.6)	11 (9.7)	1 (4.3)	0.70	10 (11.6)	32 (13.9)	9 (21.4)	0.32	0.12	1	0.27	0.08
Thalassemia	1 (2.3)	5 (4.4)	1 (4.3)	1	1 (1.2)	7 (3.0)	1 (2.4)	0.79	0.37	1	0.54	1
Others¶	3 (7.0)	8 (7.1)	2 (8.7)	0.92	1 (1.2)	6 (2.6)	2 (4.8)	0.39	0.01	0.11	0.08	0.61
Neonatal Characteristics												
Male-no. (%)	27 (62.8)	52 (46.0)	15 (65.2)	0.07	50 (58.1)	121 (52.6)	27 (64.3)	0.31	0.54	0.61	0.25	0.94

* P value comparing values of preeclampsia and non-preeclampsia.
† P value comparing values of teenage pregnancy with and without preeclampsia.
‡ P value comparing values of normal age pregnancy with and without preeclampsia
§ P value comparing values of elderly pregnancy with and without preeclampsia.
¶ Others underlying diseases including HIV, syphilis, epilepsy, asthma , migraine, viral hepatitis, allergic rhinitis, thyroid disease and heart disease.

had the highest body mass index (median 30.2, IQR 27.0 to 33.5; P=0.007). While the group of elderly pregnancy had the highest pre-delivery weight (median 76.9, IQR 62.0 to 84.0; P=0.032). Nevertheless, gestational age, height, type of delivery, history of smoking and alcohol drinking, anemia, thalassemia, and others underlying diseases of the three studied groups were likely to be similar.

For those without the diagnosis of preeclampsia, the group of teenage pregnancy had the highest gestation age (median 39.0, IQR 38.0 to 39.6; P=0.013) and the highest proportion of nulliparous (79.1%; P<0.001). While the group of the elderly pregnancy had the highest body mass index (median 27.3, IQR 25.2 to 29.7; P=0.019). However, age, term, preterm, abort, alive, height, pre-delivery weight, cesarean section, smoking, alcohol drinking, neonatal characteristic, anemia, thalassemia, and other underlying diseases tended to be similar across the three groups.

OUTCOMES

In the preeclampsia group, there were no significant differences among the three groups regarding birth weight in teenage pregnancy, normal age pregnancy and elderly pregnancy (median weight, 2,860 g (IQR 2,200 to 3,230); median weight, 2,910 g (IQR 2,525 to 3,220) and median weight, 2,840 g (IQR 2,480 to 3,290), respectively; P=0.842) as well as other outcomes e.g., placenta previa, turbidity of amniotic fluid, blood loss, APGAR score at 1 minute, APGAR score at 5 minute, perinatal asphyxia and congenital anomalies (Table 2). However, the proportion of

Table 2. Pregnancy outcomes

Outcome	Preeclampsia				No Preeclampsia							
	Teenage pregnancy	Normal age pregnancy	Elderly pregnancy	P Value	Teenage pregnancy	Normal age pregnancy	Elderly pregnancy	P Value	P Value*	P Value†	P Value‡	P Value§
Primary Outcome												
Birth weight-gm				0.84				0.25	<0.001	0.08	<0.001	0.1
Median	2.86	2.91	2.84		3.00	3.11	3.1					
Interquartile range	2.20-3.23	2.53-3.22	2.48-3.29		2.79-3.30	2.84-3.40	2.79-3.43					
Secondary Outcome												
Placenta Previa-no. (%)	0	0	1 (4.3)	0.033	0	0	1 (2.4)	0.117	1	N/A	<0.001	1
Turbidity of amniotic fluid-no. (%)				0.909				0.875	0.001	0.608	0.001	0.557
Clear	36 (83.7)	90 (61.6)	20 (13.7)		75 (87.2)	208 (90.4)	39 (92.9)					
Mild meconium	3 (7.0)	8 (66.7)	1 (8.3)		7 (8.1)	15 (6.5)	2 (4.8)					
Thick meconium	4 (9.3)	15 (71.4)	2 (9.5)		4 (4.7)	7 (3.0)	1 (2.4)					
Blood loss-ml				0.424				0.082	0.007	0.15	0.021	0.916
Median	150	200	200		150	150	175					
Interquartile range	150-300	150-300	150-300		150-200	150-300	150-400					
APGAR score-no.												
At 1 min				0.258				0.489	<0.001	<0.001	<0.001	0.251
Median	9	9	9		9	9	9					
Interquartile range	8 -9	8 -9	7-10		9-10	9-10	9-10					
At 5 min				0.848				0.937	<0.001	0.008	<0.001	0.168
Median	10	10	10		10	10	10					
Interquartile range	9-10	9-10	9-10		10-10	10-10	10-10					
Perinatal asphyxia-no. (%)	7 (16.3)	17 (15.0)	3 (13.0)	0.94	4 (4.7)	7 (3.0)	3 (7.1)	0.354	<0.001	0.041	<0.001	0.657
Congenital anomalies-no. (%)	0	2 (1.8)	0	1	1 (1.2)	0	0	0.358	0.259	1	0.108	N/A

* P value comparing values of preeclampsia and non-preeclampsia.
† P value comparing values of teenage pregnancy with and without preeclampsia.
‡ P value comparing values of normal age pregnancy with and without preeclampsia
§ P value comparing values of elderly pregnancy with and without preeclampsia.
¶ Others underlying diseases including HIV, syphilis, epilepsy, asthma , migraine, viral hepatitis, allergic rhinitis, thyroid disease and heart disease.

mothers with placenta previa was highest in the elderly pregnancy group (P=0.033).

In those without preeclampsia, there were no significant differences among the three groups regarding birth weight in the teenage, normal age and elderly pregnancy groups (median birth weight, 3,000 g (IQR 2,790 to 3,300); median birth weight 3,105 g (IQR 2,840.0 to 3,402.5) and median birth weight 3,080 g (IQR 2,790 to 3,430), respectively; P=0.253) as well as other outcomes e.g., placenta previa, turbidity of amniotic fluid, blood loss, APGAR score at 1 minute, APGAR score at 5 minute, perinatal asphyxia and congenital anomalies.

In mothers with preeclampsia compared to those without preeclampsia, it found that the former group tended to have lower birth weight (median birth weight, 2,900 g (IQR 2,480 to 3,230) vs. median birth weight, 3,060 g (IQR 2,820 to 3,370); P<0.001), higher proportion of thick meconium of amniotic fluid (11.7% vs. 3.4%; P=0.001), more blood loss (median blood loss, 200 ml (IQR 150 to 300) vs. median blood loss, 150 (IQR 150 to 300); P=0.007), lower APGAR score at 1 minute (median score, 9 (IQR 8 to 9) vs. median score, 9 (IQR 9 to 10); P<0.001), tended to have lower APGAR at 5 minute (median score, 10 (IQR 9 to 10) vs. median score, 10 (IQR 10 to 10); P<0.001) and tended to have higher proportion of perinatal asphyxia (15.1% vs. 3.9%;P<0.001).

In the group of teenage pregnancy with preeclampsia compared to those without preeclampsia, it found that the former group had no significant differences between the two groups regarding birth weight as well as other outcomes e.g., placenta previa, the turbidity of the amniotic fluid, blood loss, perinatal asphyxia and congenital anomalies. However, the group of teenage pregnancy with preeclampsia tended to have lower APGAR score at 1 minute (median score, 9 (IQR 8 to 9) vs. median score, 9 (IQR 9 to 10); P<0.001), lower APGAR score at 5 minute (median score, 10 (IQR 9 to 10) vs. median score, 10 (IQR 10 to 10); P=0.008), higher proportion of perinatal asphyxia (16.3% vs. 4.7%; P=0.041).

In the group of normal age pregnancy with preeclampsia compared to those without preeclampsia, it found that the former group tended to have lower birth weight (median birth weight, 2,910 g (IQR 2,525.0 to 3,220.0) vs. median birth weight, 3,105.0 g (IQR 2,840.0 to 3,402.5); P<0.001)), higher proportion of thick meconium (71.4% vs. 3.0%, respectively (P=0.001)), tended to have higher blood loss (median blood loss, 200 ml (IQR 150 to 300) vs. 150 ml (IQR 150 to 300); P=0.021)), lower APGAR score at 1 minute (median score, 9 (IQR 8 to 9) vs. median score, 9 (IQR 9 to 10); P<0.001)), lower APGAR score at 5 minute (median score, 10 (IQR 9 to 10) vs. 10 (IQR 10 to 10); P<0.001)), higher proportion of perinatal asphyxia (15.0% vs. 3.0%; P<0.001)) and there were no significant differences between the two groups regarding other outcomes e.g., placenta previa and congenital anomalies.

In the group of elderly pregnancy with preeclampsia compared to those without preeclampsia, it found that there were no significant differences between the two groups

Table 3. Adjusted Odds Ratios of Low Birth Weight with Pregnancy Outcomes.

Factor	Low Birth Weight	Low Birth Weight
	Crude Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)
Teenage pregnancy	1.84 (1.05-3.20)	1.61 (0.76-3.42)
Elderly pregnancy	1.82 (0.89-3.70)	1.32 (0.54-3.24)
Gestational age	0.45 (0.38-0.54)	0.46 (0.38-0.56)
Body mass index	0.94 (0.88-0.99)	0.88 (0.82-0.95)
Anemia	1.09 (0.53-2.24)	1.89 (0.72-4.96)
Thalassemia	0.41 (0.05-3.14)	0.25 (0.02-2.90)
Preeclampsia	4.68 (2.79-7.86)	4.34 (2.18-8.64)

regarding birth weight as well as other outcomes e.g., placenta previa, turbidity of amniotic fluid, blood loss, APGAR score at 1 minute, APGAR score at 5 minute, perinatal asphyxia and congenital anomalies.

FACTOR ASSOCIATED WITH LOW BIRTH WEIGHT

From the bivariable analysis, the factors found to be associated with higher rate of low birth weight were teenage pregnancy (COR, 1.84; 95% CI 1.05 to 3.20), young gestational age (COR, 0.45; 95% CI 0.38 to 0.54), low body mass index (COR, 0.94; 95% CI, 0.88 to 0.99) and preeclampsia (COR, 4.68; 95% CI 2.79 to 7.86), However, from the logistic regression, it found that young gestational age (AOR, 0.46; 95% CI 0.38 to 0.56) and low body mass index (AOR, 0.88; 95% CI, 0.82 to 0.95) decreased the chance of having low birth weight infant while preeclampsia (AOR, 4.34; 95% CI, 2.18 to 8.64) increased the chance of having low birth weight infants. Nonetheless, teenage pregnancy, elderly pregnancy, anemia, and thalassemia seemed not to be associated with low birth weight.

DISCUSSION

MAJOR FINDINGS

In those with preeclampsia, there were no significant differences among the three maternal age groups regarding infantile birth weight. In the those without preeclampsia, there were also no significant differences among the three maternal age groups regarding infantile birth weight. For teenage and elderly pregnancies, those with preeclampsia tended to have lower infantile birth weight. Moreover, factors found to be associated with higher rate of low birth weight included young gestational age, low body mass index and preeclampsia.

STRENGTH AND LIMITATION

To our knowledge, this is the first study examining the relationship between maternal age group with preeclampsia and infantile birth weight. A major strength of this study is that we completely collected data by retrieving and reviewing patient medical records. However, more case and control patients are still required. Moreover, selection

bias, missing data were unavoidable due to the retrospective nature of the study design.

COMPARISON WITH OTHER STUDIES

In the present study, perinatal asphyxia significantly increased in mothers with preeclampsia, this correlated with the findings from previous study showed that perinatal asphyxia is significantly more frequent following any kinds of maternal hypertensive disorder compared to the control group.[10] The present study found that lower APGAR score at 1 and 5 minute were significantly more frequent in mothers with preeclampsia compared to those without preeclampsia. Our findings were in accordance with the results of the study performed in 2005 reported that low APGAR score was significantly found more frequently in women with severe preeclampsia when compared to women with mild preeclampsia and women with normotensive.[7] According to the present study, preeclampsia increased the chance of having low birth weight infants, this was similar to previous studies mentioned that pregnancies complicated by preeclampsia, are characterized by an increased rate of low birth weight infants, compared with normal pregnancies.[3,9,10] Our study showed that teenage and elderly pregnancy seemed not to be associated with low birth weight infants. Nevertheless, the studies from the United Kingdom, Taiwan, and the United States showed that teenage pregnancy was likely to have low birth weight infants whereas elderly pregnancy was liable to be not.[11-13] Our study showed that low gestational age tended to increase low infantile birth weight. Similarly, the previous studies showed that lower gestational age increases the chance of having low birth weight infant.[14-18] In the present study, mothers with anemia did not increase the chance of having low birth weight and this agreed with the studies from New York and southern Benin.[19-20] Our study showed that mothers with thalassemia were not associated with low birth weight, nevertheless, the previous study showed that mothers with thalassemia tended to increase low birth weight infants.[21] This might be due to the smaller of our study. In the present study, gestational age was not significantly different between those with and without preeclampsia, however, the studies showed that gestational age in preeclampsia group was significantly younger than the control group.[22] Caesarean delivery rate was not significantly different between the two groups in the present study and one study from Sweden.[23] However, increased rate of caesarean delivery is reported in some studies.[24-27]

CONCLUSION AND IMPLICATION

In conclusion, maternal age group was not associated with infantile birth weight in both those with and without preeclampsia. However, gestational age and body mass index decreased the chance of having low birth weight infants while preeclampsia increased the chance of having low birth weight infants. Further studies are needed to determine the association between subgroup of preeclampsia and infantile birth weight by maternal age group and should increase the sample size of the study population.

ACKNOWLEDGMENTS & DECLARATION

The authors would like to thank :Thammasorn Jeeraaumponwat, M.D, Ph.D. for their supervision. We also would like to thank Khon Kaen Medical Education Center, Khon Kaen Hospital for their supports.

COMPETING INTERESTS: This study has no competing on interest.
FUNDING: None

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Central venous catheter-related bloodstream infection in the non-intensive care unit

ORIGINAL ARTICLE BY

Warin Puangpoo[1], M.D., Sarocha Angwittayatorn[2], M.D., Thidarat Chaisiwamongkol[3], M.D., Narutsama Pimpanit[4], M.D.,

[1]Nongrua Hospital, Thailand, [2]Si Wilai Hospital, Thailand, [3]Ban Phai Hospital, Thailand, [4]Rong Kham Hospital, Thailand

Accepted: January 2016
Latest revision: March 2017
Printed: April 2017

Correspondence to: Thidarat Chaisiwamongkot; t.chaisiwamongkol@gmail.com

ABSTRACT

OBJECTIVE

To compare the rates of central venous catheter-related bloodstream infections in the ICU (intensive care unit) and non-ICU.

METHODS

We conducted a retrospective cohort study who had been admitted to Khon Kaen Hospital from December 2011 to September 2013. The primary outcome was the rate of central venous catheter-related bloodstream infections. The secondary outcomes were the causative organisms, length of hospital stay and death.

RESULTS

There were 330 patients in the analysis; 173 were non-ICU and 157 were ICU patients. The rates of central venous catheter-related bloodstream infection were similar among the ICU and non-ICU settings (HR, 0.59; 95% CI, 0.28 to 1.27) as well as the mortality rate (HR, 0.94; 95% CI, 0.61 to 1.46). The length of hospital stay was significantly longer in the ICU patients than those of non-ICU patients ($P<0.001$). From the Cox proportional hazard regression, it found that catheter insertion through femoral vein and SAPS II score above 40 had significantly increased the risk of central venous catheter-related bloodstream infection (HR 25.00, 95% CI 3.48 to 179.53; HR 5.47, 95% CI 1.51 to 19.85, respectively)

CONCLUSION

there was no evidential difference in terms of the rates of central venous catheter-related bloodstream infection and mortality between the non- ICU and ICU patients. Catheter insertion through the femoral vein and SAPS II score above 40 increased the risk of central venous catheter-related bloodstream infections.

INTRODUCTION

Bloodstream infections is still a leading cause of morbidity and mortality in the United States.[1] Most of the cases are associated with the central venous catheter, especially patients in the intensive care unit (ICU).[2] The United States National Healthcare Safety Network (NHSN) reported that the overall catheter-related bloodstream infections rate were 1.5 per 1,000 catheter-days for 2006 through 2008.[3] A study conducted in the UK reported similar data with the hospital-acquired bloodstream infection rates from 2.8 to 5.4 per 1,000 catheter-days.[4] Catheter-related bloodstream infections have a considerable effects on morbidity and mortality of the patient as well as hospital resources as it can prolong length of hospital stay and it also increases the overall medical costs per hospitalization.[5,6,7,8,9,10,11]

There are limited data on catheter-related bloodstream infections outside of the ICU, partly due to the perception of high usage of central venous catheters in the ICU while the majority of central venous catheters insertion as high as 70% is done outside the ICU setting.[12] According to a previous study, the estimated rate of central venous catheter-related bloodstream infection in non-ICU is 8.9 per 1000 catheter-days.[13] However, the rates of central venous catheter-related bloodstream infections among ICU and non-ICU patients have not been directly compared. Thus, we conducted this study to compare the rates of central venous catheter-related bloodstream infections in two different settings; ICU and non-ICU. Moreover, we also aimed to define and compare the microbiological pattern of causative organisms in two different settings as mentioned above.

METHODS

STUDY DESIGN

We conducted a retrospective cohort study to compare the rates of central venous catheter-related bloodstream infection between ICU and that of non-ICU patients who had been admitted to Khon Kaen Hospital from December 2011 to September 2013.

PATIENTS

We confined our retrospective cohort study to all 730 patients admitted to Khon Kaen Hospital receiving central venous catheter between December 2011 and September 2013.Their medical records were reviewed. All patients receiving central venous catheters were included. Pediatric (under 15 year-old) patients, patients with positive hemoculture prior to catheter insertion, positive hemoculture within 48 hrs after catheter insertion, catheter insertion prior to admission, catheter removal within 48 hrs after insertion, death within 48 hrs after catheter insertion and whom had been discharged against medical advice within 48 hrs after insertion were excluded. Incomplete medical records were as well excluded. We divided patients into two groups; ICU and non-ICU patients. Diagnosis of catheter-

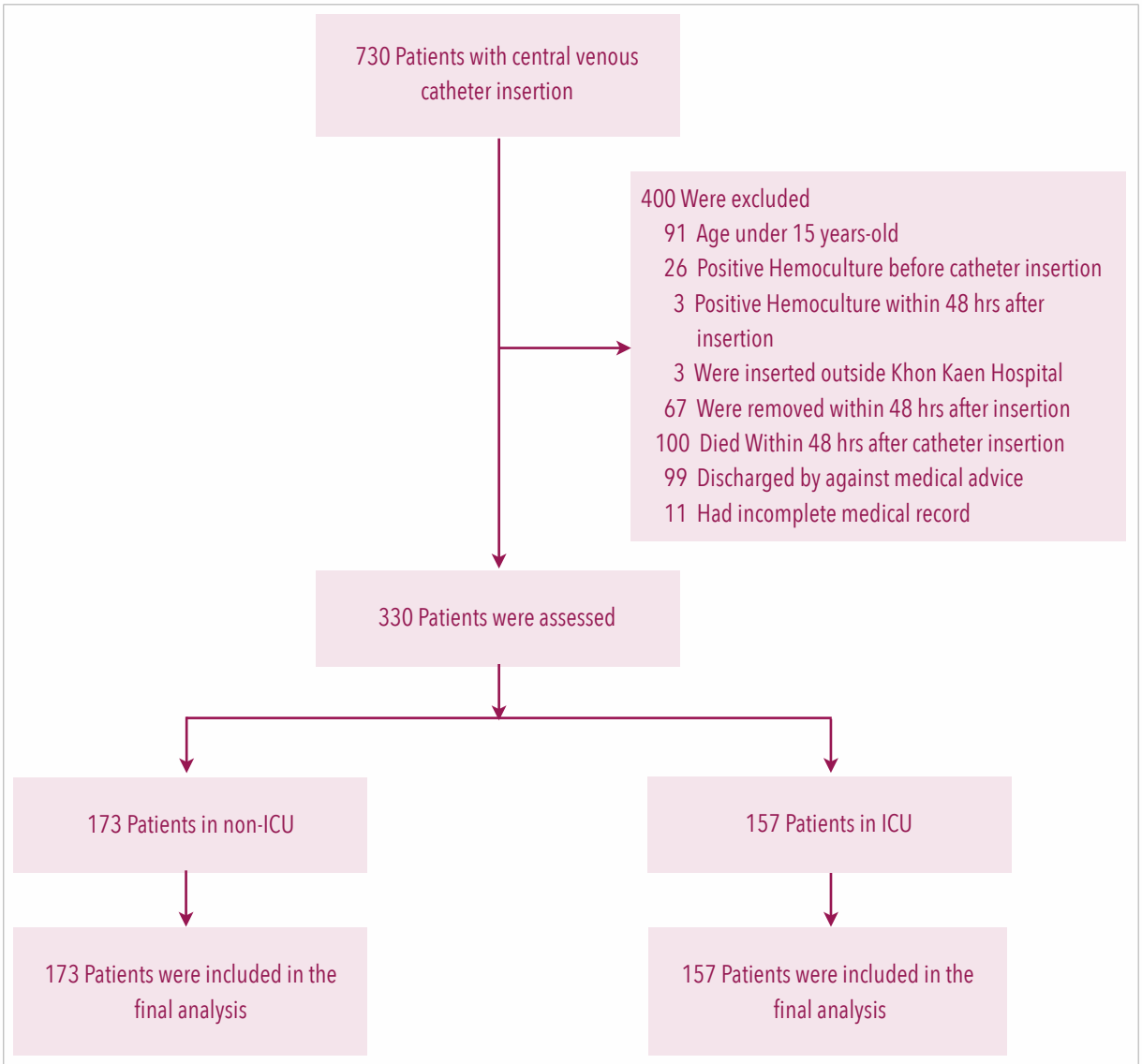

Figure 1. Study Flow

related bloodstream infection was based on the presence of bloodstream infection without other apparent sources of infection. Microbiological confirmation of catheter-related bloodstream infection was made by catheter tip and blood cultures, meeting one of the following criteria (i) positive of cultures of the same organism from both the catheter tip and at least one percutaneous hemoculture or (ii) positive cultures of the same organism from at least two blood samples meeting criteria for quantitative blood culture or different time to positive.[14]

DATA COLLECTION

Variables including gender, age, primary diagnosis at admission, underlying disease, catheter cavity, anatomical site, central venous catheter insertion site, number of catheter, indication for central venous catheter insertion, number of applied antibiotics, duration of central venous catheter use and SAPS II score were reviewed and collected from the included medical records.

OUTCOME MEASUREMENT

The primary outcome of this study was the rate of central venous catheter-related bloodstream infections. Secondary outcomes including the causative organisms, the length of stay and death were recorded.

STATISTICAL ANALYSIS

For descriptive statistics, categorical variables were summarized as number and percent (%). For scale variables, mean and standard deviation (SD) were used if they were normally distributed while median and interquartile range (IQR) were used if they were non-normally distributed. For inferential statistics, chi-square was used for categorical variables. T-test and Mann-Whitney U test were used for normally and non-normally distributed variables, respectively. We used Mann-Whitney U test for the analysis of age and duration of central venous catheter use. On the other hand, chi-square was used for the analysis of sex, primary diagnosis at admission, underlying disease, catheter cavity, anatomical site, central venous catheter insertion site, number of catheters, indication for central venous catheter insertion, number of applied antibiotics and SAPS II score. Outcomes including the rates of central venous catheter-related bloodstream infections, the length of hospital stay and death were interpreted using hazard ratio (HR) with its 95% confidence interval (CI). Factors determining infection were identified through Cox proportional hazard regression and interpreted using adjusted hazard ratio (HR) and its 95% CI.

RESULTS

PATIENTS

In the present study, 730 patients who have been inserted with central venous catheters between December 2011 and September 2013 in Khon Kaen Hospital were preliminarily included. However, 400 patients were excluded and left a total of 330 for the analysis (Figure 1). In general, most of them were male (59.7%) with the average age of 58 years. One hundred and fifty-seven out of 330 were ICU-patients and 173 were non-ICU patients (Table 1).

Comparing between those admitted in the ICU and non-ICU, the former group tended to have more proportion of patients with the cardiovascular condition ($P<0.001$), trauma ($P=0.015$), triple lumen catheter ($P<0.001$), Swan-Ganz catheter ($P<0.001$), central venous catheter inserted through subclavian vein ($P=0.014$), catheter insertion in the ICU ($P<0.001$), catheter insertion in the operating room ($P<0.001$), two catheters ($P<0.001$) and catheter insertion for intravenous fluid or antibiotics ($P<0.001$). Moreover, the median duration of central venous catheter use was higher

Table 1. Characteristics of the patients

Characteristic	Total	Non-ICU	ICU	P Value
Age-yr				0.211
Median	58	59	58	
Interquartile range	44.8-67.0	47.5-69.5	43.5-66.5	
Male sex-no. (%)	197 (59.7)	103 (59.5)	94 (59.9)	0.951
Primary diagnosis at admission-no. (%)†				
Cardiovascular condition	99 (30.0)	21 (12.1)	78 (49.7)	<0.001
Central nervous condition	11 (3.3)	6 (3.5)	5 (3.2)	0.886
Hepatopancreatobiliary condition	17 (5.2)	11 (6.4)	6 (3.8)	0.298
Gastrointestinal condition	52 (15.8)	41 (23.7)	11 (7.0)	<0.001
Genitourinary condition	37 (11.2)	32 (18.5)	5 (3.2)	<0.001
Malignant tumor	21 (6.4)	12 (6.9)	9 (5.7)	0.655
Infection	103 (31.2)	63 (36.4)	40 (25.5)	0.032
Respiratory condition	40 (12.1)	18 (10.4)	22 (14.0)	0.316
Trauma*	9 (2.7)	1 (0.6)	8 (5.1)	0.015
Obstetric and gynecological condition*	1 (0.3)	1 (0.6)	0	1
Other	18 (5.5)	11 (6.4)	7 (4.5)	0.448
Underlying disease-no. (%)†				
Diabetes mellitus	82 (24.8)	48 (27.7)	34 (21.7)	0.201
Hematological malignancy*	5 (1.5)	3 (1.7)	2 (1.3)	1
Renal disease	39 (11.8)	31 (17.9)	8 (5.1)	<0.001
Catheter type-no. (%)†				
Single lumen	20 (6.1)	14 (8.1)	6 (3.8)	0.104
Double lumen	233 (70.6)	147 (85.0)	86 (54.8)	<0.001
Triple lumen	78 (23.6)	13 (7.5)	65 (41.4)	<0.001
Swan-Ganz	20 (6.1)	2 (1.2)	18 (11.5)	<0.001
Anatomical site-no. (%)				
Subclavicular vein	22 (6.7)	6 (3.5)	16 (10.2)	0.014

Table 1. (Continued)

Characteristic	Total	Non-ICU	ICU	P Value
Internal jugular vein	288 (87.3)	152 (87.9)	136 (86.6)	0.736
Femoral vein	28 (8.5)	18 (10.4)	10 (6.4)	0.189
External jugular vein*	6 (1.8)	2 (1.2)	4 (2.5)	0.429
Place of line insertion-no. (%)				
Intensive care unit	79 (23.9)	4 (2.3)	75 (47.8)	<0.001
Conventional ward	149 (45.2)	134 (77.5)	15 (9.6)	<0.001
Surgery room	91 (27.6)	24 (13.9)	67 (42.7)	<0.001
Emergency department	12 (3.6)	11 (6.4)	1 (0.6)	0.006
No. of catheter-no. (%)				
1	214 (64.8)	144 (83.2)	70 (44.6)	<0.001
2	100 (30.3)	24 (13.9)	76 (48.4)	<0.001
3	11 (3.3)	3 (1.7)	8 (5.1)	0.089
4*	5 (1.5)	2 (1.2)	3 (1.9)	0.672
Indication for catheter insertion-no. (%)				
Intravenous fluids/antibiotic	273 (82.7)	128 (74.0)	145 (92.4)	<0.001
Hemodialysis	40 (12.1)	28 (16.2)	12 (7.6)	0.018
Total parenteral nutrition-no. (%)	23 (7.0)	17 (9.8)	6 (3.8)	0.032
Blood filtration-no. (%)*	2 (0.6)	2 (1.2)	0	0.5
Applied antibiotic 3-no. (%)	14 (4.2)	7 (4.0)	7 (4.5)	0.853
Duration of central venous catheter use-day				<0.001
Median	10	8	12	
Interquartile range	5.0-17.0	4.5-15.0	8.0-18.0	
SAPS II score 40-no. (%)‡	110 (33.3)	56 (32.4)	54 (34.4)	0.697

* P values were calculated with the use of Fisher's exact test in trauma, obstetric and gynecology condition, hematologic malignancy, external jugular vein, four catheters and blood infiltration.

† Patients may have had more than one type of event.

‡ Simplified Acute Physiological II score (SAPS II score) over 40 represented the mortality rate over 50%.

Table 2. Clinical outcomes

	Total patients	Non-ICU patients	ICU patients	Hazard ratio
Central venous catheter-related bloodstream infection-per 1000 catheter day	3.6	4.3	2.9	0.59 (0.28-1.27)
Death-no. (%)	44 (13.3)	20 (11.6)	24 (15.3)	0.94 (0.61-1.46)
Length of hospital stay (day)				
Median	13.5	11	16	
Interquartile range	8.0-24.0	6.0-22.0	11.0-25.0	

in the former group (P<0.001). On the other hand, the former group tended to have less proportion of patients with gastrointestinal condition (P<0.001), genitourinary condition (P<0.001), infection (P=0.032), renal disease (P<0.001), double lumen catheter (P<0.001), catheter insertion in the conventional ward (P<0.001), catheter insertion in the emergency department (P=0.006), one catheter (P<0.001), catheter insertion for hemodialysis (P=0.018) and total parenteral nutrition (P=0.032). However, age, gender, other primary diagnosis including central nervous condition, hepatobiliary condition, malignant tumor, respiratory condition, obstetric and gynecological condition, other underlying diseases including diabetes mellitus and hematological malignancy tended to be similar across the two groups. Furthermore, the two groups tended to have similar proportions of patients with single lumen catheter, patients with catheters inserted through internal jugular vein, femoral vein and external jugular vein, patients with three and four catheters and patients who had received central venous catheters for blood infiltration. Moreover, both groups appeared to have similar proportions of patients receiving more than or equal to three antibiotics and those who had SAPS II score above 40.

OUTCOMES

The rates of central venous catheter-related bloodstream infection were similar among the ICU and non-ICU settings (HR, 0.59; 95% CI, 0.28 to 1.27) as well as the mortality rate (HR, 0.94; 95% CI, 0.61 to 1.46) (Table 2). The median length of hospital stay of those admitted in the ICU and non-ICU groups were 16 (IQR 11.0 to 25.0) and 11 days (IQR 6.0 to 22.0), respectively. The length of hospital stay was significantly longer in the ICU patients than those of non-ICU patients (P<0.001). From the Table 3, we found that the majority of the cases diagnosed with the central venous catheter-related infection, as high as 47.1%, were due to coagulase-negative staphylococci, followed by Candida spp. (11.8%), *Escherichia coli* (5.9%), *Acinetobacter baumannii*

(5.9%) and *Pseudomonas aeruginosa* (5.9%), respectively.

FACTORS DETERMINING CENTRAL VENOUS CATHETER-RELATED BLOODSTREAM INFECTION

From the Cox proportional hazard regression, it found that catheter insertion through femoral vein and SAPS II score above 40 had significantly increased the risk of central venous catheter-related bloodstream infection (HR 25.00, 95% CI 3.48 to 179.53; HR 5.47, 95% CI 1.51 to 19.85, respectively) (Table 4). However, the other risk factors were not found to be associated with central venous catheter-related bloodstream infections.

Table 3. Organisms Isolated in Patients with Central Venous Catheter-Related Bloodstream Infections

Organism	N=17
Gram-positive:-no. (%)	
Coagulase-negative staphylococci	8
Other Gram positive organism	4
Gram-negative:-no. (%)	
Escherichia coli	1
Acinetobacter baumannii	1
Pseudomonas aeruginosa	1
Candida spp.:-no. (%)	2

DISCUSSION

IMPORTANT FINDINGS

The rates of central venous catheter-related bloodstream infection were not significantly different between those admitted in the ICU and non-ICU patients. The majority of the cases with central venous catheter-related bloodstream infections were due to Gram-positive organisms, specifically coagulase-negative staphylococci, followed by Candida spp., *Escherichia coli*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*. There was no significant difference in the result of mortality rate among the two groups. The median length of hospital stay in ICU patients was longer than those of non-ICU patients. In our study, two factors that had been shown to increase the risk of central venous catheter-related bloodstream infections were catheter insertion through the femoral vein and SAPS II score above 40.

STRENGTH AND LIMITATION

In terms of strength of the study, our study was one of the few that aimed to assess the rate of central venous catheter-related bloodstream infection in the non-ICU setting. This study directly compared the rates of central venous catheter-related bloodstream infection between those admitted to the ICU and non-ICU patients. It had the adequate sample size and confounding factors including underlying diseases, anatomical site of insertion, indication for catheter insertion, number of applied antibiotics and SAPS II score had been well adjusted. Despite the fact that our study was a retrospective cohort study and missing data was

Table 4. Cox proportional hazard regression analysis of factors determining central venous catheter-related bloodstream infection

	Adjusted hazard ratio	95% Confidence interval
Underlying disease		
Diabetes mellitus	1.03	0.30-3.51
Renal disease	0.18	0.02-2.01
Anatomical site		
Subclavian vein	2.64	0.18-39.55
Internal jugular vein	5.97	0.61-58.07
Femoral vein	25	3.48-179.53
Indication for catheter insertion		
Intravenous fluid/antibiotics	0.08	0-3.35
Hemodialysis	0.21	0.01-6.84
Total parenteral nutrition	0.54	0.02-19.48
Applied antibiotic 3	2.94	0.41-20.97
SAPS II score above 40	5.47	1.51-19.85

expectable, only 11 patients with incomplete medical records were observed.

Limitations have to be considered in the interpretation of our results. This study was conducted as a retrospective cohort study. The data were obtained from scanned written medical records in the electronic database in which some data could be incorrect due to the recording process, itself. In some cases with central venous catheters, hemoculture and culture of the catheter tip had not been taken after catheter removal. Some laboratory results were unable to obtain due to the technical problem of the hospital system. However, we tried to retrieve all the missing data and verify all the data as much as possible. Still, the total number of the cases with central venous catheter-related infection was quite small. This affected the precision of our estimates in which can be seen from wide CI. Moreover, the validity of our result in term of microbiological pattern might not be concluded.

COMPARISON WITH OTHER STUDIES

The overall rate of central venous catheter-related bloodstream infection in our study (3.6 per 1000 catheter-days) was comparable with previous studies which reported the rate of catheter-related bloodstream infection with a range of 1.5-5.4 per 1000 catheter-days.[3,4] The rate of central venous catheter-related infection in the ICU and non-ICU

settings were 2.9 per 1000 catheter-days and 4.3 per 1000 catheter-days, respectively. The results we found were correspondent with other studies which reported the rates of central venous catheter-related bloodstream with the range of 2.2-6.6 per 1000 catheter-days in ICU and 1.9-8.9 per 1000 catheter-days in the non-ICU. [13,22,23,25,26,27]

Regarding causative organisms, the majority of the cases of central venous catheter-related bloodstream infection was due to Gram-positive organisms. Several studies reported similar results.[15,20,22,23,24,25,26] Unlike our study, the study conducted in China found that the most common organisms causing central venous catheter-related bloodstream infection were Gram negative organisms.[16] This difference might be due to the distinct distribution of pathogen in various settings and regions.

The mortality rate in this study was approximately 13.3% in general. We found that the mortality rate in the ICU and non-ICU settings were 15.3% and 11.6%, respectively but there was no significant difference between the two groups. There are limited studies that directly compared the outcome between the two groups. However, previous studies conducted to assess the central venous catheter-related bloodstream infection in the ICU settings reported higher mortality rate in the ICU setting with the range of 20-31%.[16,22,27] The difference in term of mortality rate might be due to the fact that a large number of dead patients was excluded along the process of our study.

CONCLUSION AND IMPLICATION

In conclusion, there was no evidential difference in terms of the rates of central venous catheter-related bloodstream infection between the ICU and non-ICU patients as well as the mortality rate between the two groups. However, the former group had significantly longer length of hospital stay. Moreover, catheter insertion through femoral vein and SAPS II score above 40 had been shown to increase the risk of central venous catheter-related bloodstream infection. Thus, those with high SAPS II score and those with femoral vein insertion should be under close monitoring for the higher chance of developing this type of infection. For the future study, the prospective cohort study with larger sample size is recommended to establish the microbiological pattern in central venous catheter-related bloodstream infection.

ACKNOWLEDGMENTS & DECLARATION

The authors would like to thank :Thammasorn Jeeraaumponwat, M.D, Ph.D. for their supervision. We also would like to thank Khon Kaen Medical Education Center, Khon Kaen Hospital for their supports.

COMPETING INTERESTS: This study has no competing on interest.
FUNDING: None

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Teenage pregnancy and preeclampsia in Asian Countries: a systematic review and meta-analysis

ORIGINAL ARTICLE BY

Krisanee Pansue[1], M.D., Siwanut Rattanaphibunsiri[2], M.D., Weerapong Nonthasila[3], M.D., Worawit Sittisorn[4], M.D.

[1]Nongphok Hospital, Thailand, [2]Phayakkhaphum Phisai Hospital, Thailand, [3]Kantharawichai Hospital, Thailand, [4]Phykhieo Hospital, Thailand.

Accepted: January 2016
Latest revision: March 2017
Printed: April 2017

Correspondence to: Krisanee Pansue; k.pansue@gmail.com

ABSTRACT

OBJECTIVE

To ascertain the association between teenage pregnancy and preeclampsia in Asian countries.

METHODS

This is a systematic review and meta-analysis. We searched Medline/PubMed, Scopus, ScienceDirect, and OVID databases. Case-control and cohort studies of teenage pregnancy as a risk factor of preeclampsia were included. Two authors independently selected studies to include in the meta-analysis. Methodological quality assessment of the included studies was assessed with the Newcastle-Ottawa scale (NOS) criteria. The primary outcome of interest was preeclampsia. Our secondary outcomes included both maternal and neonatal outcomes.

RESULTS

Ten studies with 19,074 patients were included. Preeclampsia was found more common in teenage mother compared with adult mother (odds ratio (OR), 2.69; 95% confidence interval (CI) 1.02 to 7.05; I^2=93%). For other maternal outcomes, teenage pregnancy also increased the risk for developing anemia (OR, 1.20; 95% CI, 1.03 to 1.41; I^2=52%), while it decreased the risk for cesarean delivery (OR, 0.65; 95% CI, 0.47 to 0.89; I^2=89%), gestational diabetes mellitus (OR, 0.45; 95% CI, 0.34 to 0.61; I^2=0%). For the neonatal outcomes, teenage pregnancy also increased the risk for preterm birth (OR, 2.30; 95% CI, 1.60 to 3.30; I^2=84%), intrauterine growth retardation (OR, 1.64; 95% CI, 1.40 to 1.93; I^2=0%) and low birthweight (OR, 1.70; 95% CI, 1.41 to 2.06; I^2=0%).

CONCLUSION

In Asian countries, preeclampsia was found more common in teenage pregnancy compared with adult pregnancy. However, our conclusion was based on high heterogeneity of the findings and relatively poor methodological studies.

INTRODUCTION

Globally, around 16 million adolescent girls get pregnant and 95% of these happen in the developing world while maternal conditions in adolescents contribute to 13% of maternal deaths annually.[1] Pregnancies in adolescents have an increased incidence of medical and obstetric complications.[2] The frequently reported complications include preterm labor, intrauterine growth retardation, low birth weight, cesarean delivery, gestational diabetes mellitus and preeclampsia.[3-10]

Preeclampsia is a syndrome involving both mother and child with the combination of clinical and laboratory findings.[11] Women who develop preeclampsia are increased risk for various complication including seizures, pulmonary edema, organ failure, cerebral hemorrhage or even death.[12-16] Many studies have shown that teenage pregnancy increases incidence of preeclampsia compared with those with normal age pregnancy, however, this is not conclusive as many studies also have shown no differences regarding incidence of preeclampsia between those with teenage and normal age pregnancy.[7,17-20]

Asian countries have a large proportion of young people in the world and teenage pregnancy has emerged as one of the major public health problems in these countries.[21] Thus, we conducted a systematic review to assess the association between teenage pregnancy and preeclampsia in Asian countries.

METHODS

SEARCH STRATEGIES

Our search was conducted to identify published case-control and cohort studies that tried to establish the association between teenage pregnancy and preeclampsia through PubMed/MEDLINE using combinations of search Medical Subject Heading (MesH) terms; ("Pregnancy in Adolescence"[Mesh]) AND "Pre-Eclampsia"[Mesh]. For Scopus, we used the following combination of keywords; teenage pregnancy AND preeclampsia, teenage pregnancy AND pre-eclampsia, adolescent pregnancy AND preeclampsia, and adolescent pregnancy AND pre-eclampsia. In ScienceDirect, we used search the terms of teenage pregnancy and preeclampsia. In OVID we used the search algorithm; teenage pregnancy and preeclampsia in the article title or abstract or keywords search in August 2013 with no time limit for all databases. We also reviewed the reference lists of retrieved articles to identify studies that were not obtained from the preliminary literature searches. We confined our search to English language publications. Reference lists from studies selected by electronic searching were screened to identify further relevant study.

TYPES OF PARTICIPANTS

Pregnant adolescent girls aged younger than 20 years compared with adult pregnant women aged 20-34 years and both groups were singleton pregnancy.

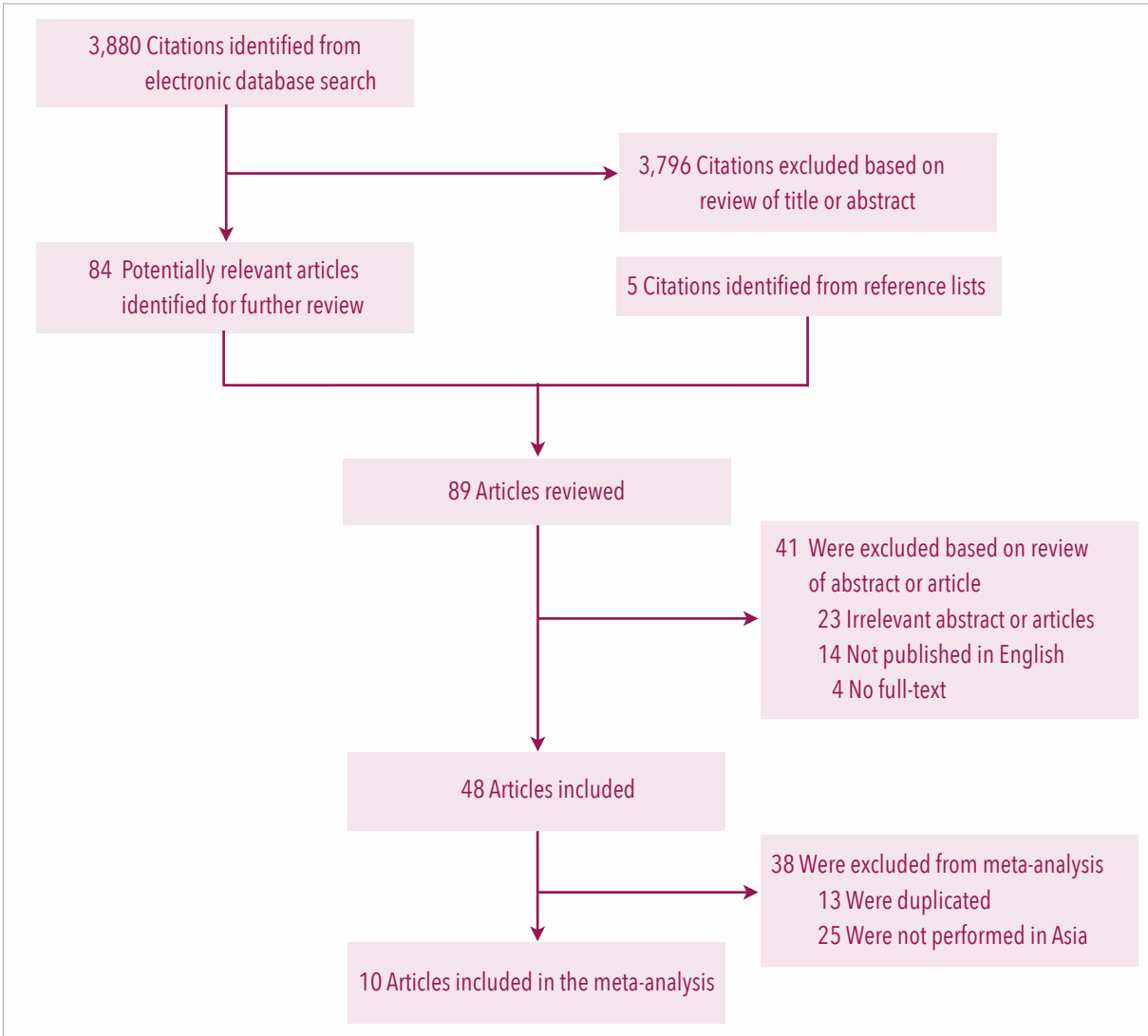

Figure 1. Flow diagram of search strategy to identify relevant studies

TYPES OF STUDIES

The articles were screened by title and abstract. Four review authors analyzed and decided independently to include all the potential studies identified as a result of the search strategy. Differences between reviewers were determined by discussion. There were the criteria we used to determine relevant studies for our review; the study had to (i) be a case-control or cohort study, (ii) include both teenage pregnant women aged younger than 20 years and a comparison group of pregnant adults aged 20-34 years with singleton

delivery, (iii) consider preeclampsia as an outcome and (iv) present the results for each group separately. Studies were excluded if they were not English, no retrievable full-text, duplicated and were not performed in Asian countries.

STUDY OUTCOMES

The primary outcome was preeclampsia diagnosed during their pregnancies. The secondary outcomes were divided into two categories; (i) maternal outcomes including anemia, premature rupture of membranes, cesarean delivery, placenta previa, gestational diabetes mellitus, operative vaginal delivery, placenta abruption, and postpartum hemorrhage and (ii) fetal outcomes including preterm birth, intrauterine growth retardation, low birth weight, breech presentation, and neonatal asphyxia.

QUALITY ASSESSMENT

Four reviewers independently assessed the quality of each study using a form derived from the Newcastle-Ottawa Scale (NOS) criteria to the recommendations of the Cochrane Collaboration and examine the following; comparability; outcome (cohort study) or exposure (case-control study). Four reviewers independently gave a quality rating to each included study; our results were compared and our differences were discussed until consensus was obtained.

DATA EXTRACTION AND MANAGEMENT

We extracted data from all of the included studies regarding authors' names, publication year, study country, study design, a number of patients who met the criteria, and a number of events for outcomes of interest.

STATISTICAL ANALYSIS AND META-ANALYSIS

Extracted data were analyzed using Review Manager (RevMan) 5.2. Data was presented as odds ratios (OR) with 95% confidence intervals (CI). For evaluation of heterogeneity we used both the chi-square test and the I^2 test, and if I^2>50%, a random effects meta-analysis was used. Assessment of publication bias was carried out by generating a funnel plot.

RESULTS

CHARACTERISTICS OF ELIGIBLE STUDIES

Overall, 3,880 titles and abstracts were initially identified (Figure 1). Later, 84 citations were selected for further review. Additional five articles were identified from reference lists. In our reviewing process, 79 articles were excluded with given reasons in Figure 1. In total, 10 eligible studies, one prospective cohort studies, six retrospective cohort studies, and three case-control studies were included in the meta-analysis. These studies included 19,074 patients. Table 1 lists the characteristics of the included studies.

METHODOLOGICAL QUALITY ASSESSMENT

One of the 10 studies scored nine for methodological quality on the NOS, six scored eight, two scored seven and one scored five (Figure 2)

Table 1. Detail of the included studies

Country	Study design	Study period	Teenage mothers		Adult mothers		Preeclampsia	
			Number	Age	Number	Age	Teenage mothers	Adult mothers
T.T.Lao and L.F.Ho, 1998[18]								
Hong Kong	Retrospective cohort	N/A	382	≤19	382	20-34	20	22
S.Ziadeh, 2001[25]								
Jordan	Retrospective cohort	1997–1999	760	<19	760	20-29	40	44
A.Abu-Heija et al, 2002[22]								
Saudi Arabia	Retrospective cohort	1996–2000	102	≤17	102	20–24	5	3
A.Moini et al, 2002[28]								
Iran	Retrospective cohort	1999-2000	312	<20	516	20-29	4	29
M.Usta et al, 2008[17]								
Lebanon	Retrospective cohort	1994-2003	486	≤19	486	25-30	14	1
K.Maryam and S.Ali, 2008[26]								
Iran	Retrospective cohort	2003-2005	1232	≤ 19	9120	20-29	22	14
E.Kovavisarach et al, 2010[23]								
Thailand	Prospective cohort	2006-2007	750	<20	750	20-34	143	15
S.Thato et al, 2007[24]								
Thailand	Case-control	2001-2003	401	≤19	815	20-34	7	22
V.Phupong and K.Suebnukarn, 2007[29]								
Thailand	Case-control	1994-2004	121	≤15	121	20-29	10	2
A.Kumar et al, 200727								
India	Case-control	N/A	396	≤19	1107	20-30	16	3

PRIMARY OUTCOME

Preeclampsia was reported in all eligible studies; 281 events in 4,915 teenage mothers were reported vs. 155 events in 14,159 adult mothers. From the meta-analysis, we found that preeclampsia was significantly more common in teenage mother compared with that of the adult mother (OR, 2.69; 95% CI, 1.02 to 7.05; I^2=93%) (Figure 3)

SECONDARY OUTCOMES

Maternal outcomes

Anemia

Anemia was reported in six eligible studies. Overall, 450 events in 2,713 teenage mothers were reported vs. 901 events in 4,096 adult mothers. Our meta-analysis showed that anemia was found significantly more common in teenage mother compared with that of the adult mothers

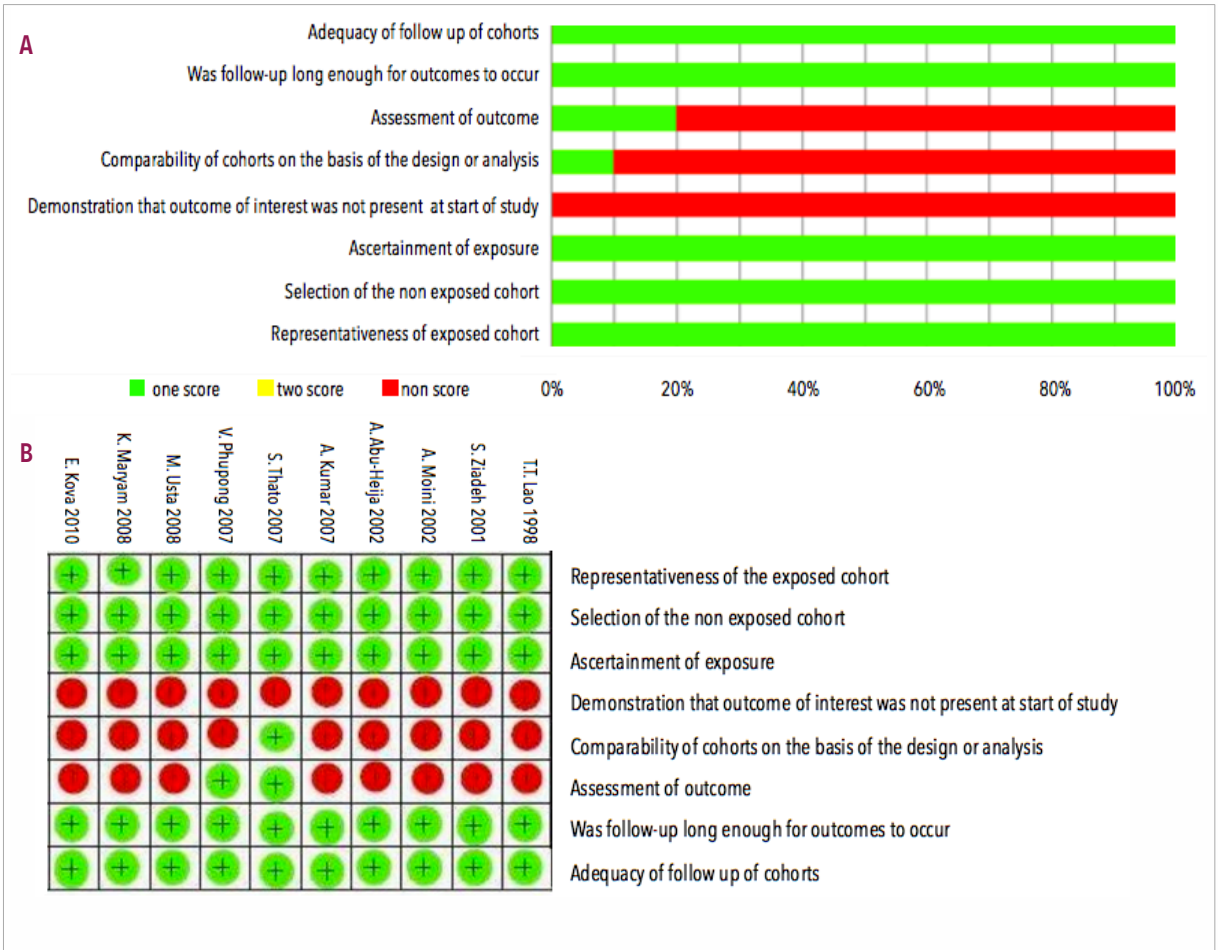

Figure 2. Newcastle-Ottawa Quality
Panel A, review authors' judgements about each item presented as percentages across all included studies; Panel B, review authors' judgements about each item for each included study

(OR, 1.30; 95% CI, 1.01 to 1.66; I^2=52%) (Figure 4, Panel A).

Premature rupture of membrane

Premature rupture of membrane was reported in five eligible studies. Overall, 207 events in 2,499 teenage mothers were reported vs. 281 events in 2,499 adult mothers. We found that the rates of premature rupture of membrane rate were similar in both groups; (OR, 0.60; 95% CI, 0.36 to 1.00; I^2=82%) (Figure 4, Panel B).

Cesarean delivery

Cesarean delivery was reported in nine eligible studies. Overall, 747 events in 4,813 teenage mothers were reported vs. 2,627 events in 14,057 adult mothers. We found that the cesarean delivery was significantly less common in teenage

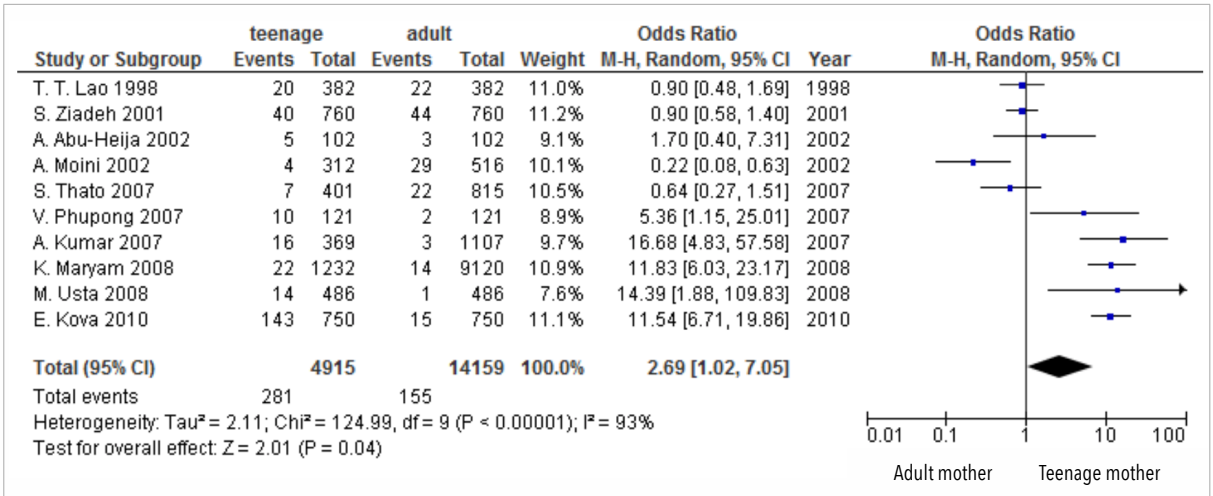

Figure 3. Forest plot of primary outcome (preeclampsia) in teenage mothers vs. normal adult mothers

mother compared with that of the adult mother (OR, 0.65; 95% CI, 0.47 to 0.89; I^2=89%) (Figure 4, Panel C).

Placenta previa

Placenta previa was reported in four eligible studies. Overall, 16 events in 2,869 teenage mothers were reported vs. 53 events in 11,171 adult mothers. We found that the rates of placenta previa were similar in both groups (OR, 0.56; 95% CI, 0.31 to 1.00; I^2=0%) (Figure 4, Panel D).

Gestational diabetes mellitus

Gestational diabetes mellitus was reported in five eligible studies. Overall, 68 events in 2,747 teenage mothers were reported vs. 144 events in 3,485 adults mothers. We found that gestational diabetes mellitus was significantly less common in teenage mother compared with that of the adult mother (OR, 0.45; 95% CI, 0.34 to 0.61; I^2=0%) (Figure 4, Panel E).

Operative vaginal delivery

Operative vaginal delivery was reported in eight eligible studies. Overall, 333 events in 3,371 teenage mothers were reported vs. 492 events in 4,523 adult mothers. We found that the rates of operative vaginal delivery were similar in both groups (OR, 0.74; 95% CI, 0.49 to 1.13; I^2=83%) (Figure 4, Panel F).

Placenta abruption

Placenta abruption was reported in five eligible studies. Overall, 15 events in 2,882 teenage mothers were reported vs. 99 events in 10,974 adult mothers. We found that the rates of placenta abruption were similar in both groups (OR, 0.86; 95% CI, 0.08 to 9.16; I^2=86%) (Figure 4, Panel G).

Postpartum hemorrhage

Postpartum hemorrhage was reported in four eligible studies. Overall, 62 events in 2,378 teenage mothers were reported vs. 59 events in

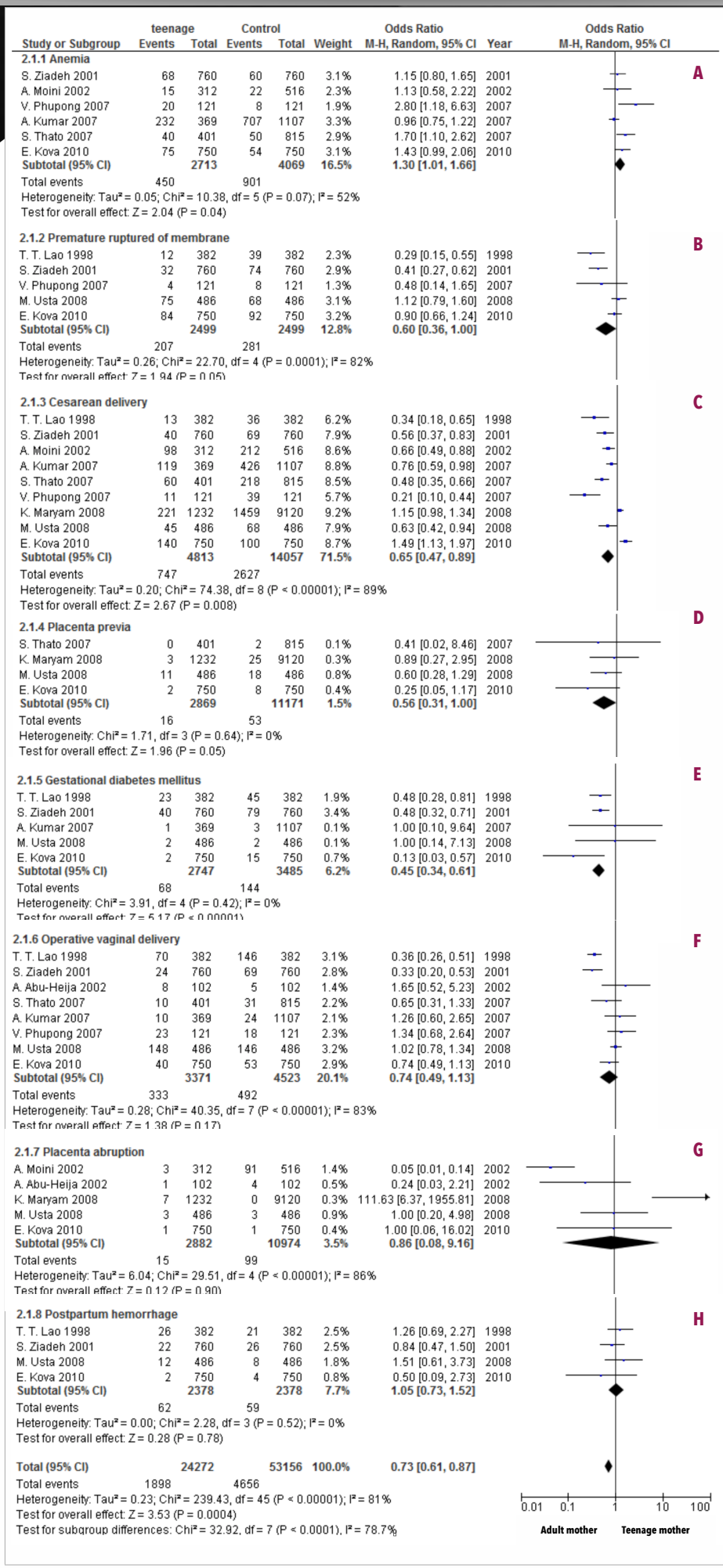

Figure 4. Meta-analysis of the included studies showing secondary outcomes on teenage mothers vs. adult mothers.
Maternal outcomes included Panel A, anemia; Panel B, premature rupture of the membrane; Panel C, cesarean delivery; Panel D, placenta previa; Panel E, gestational diabetes; Panel F, operative vaginal delivery; and Panel G, placenta abruption and; Panel H, postpartum hemorrhage

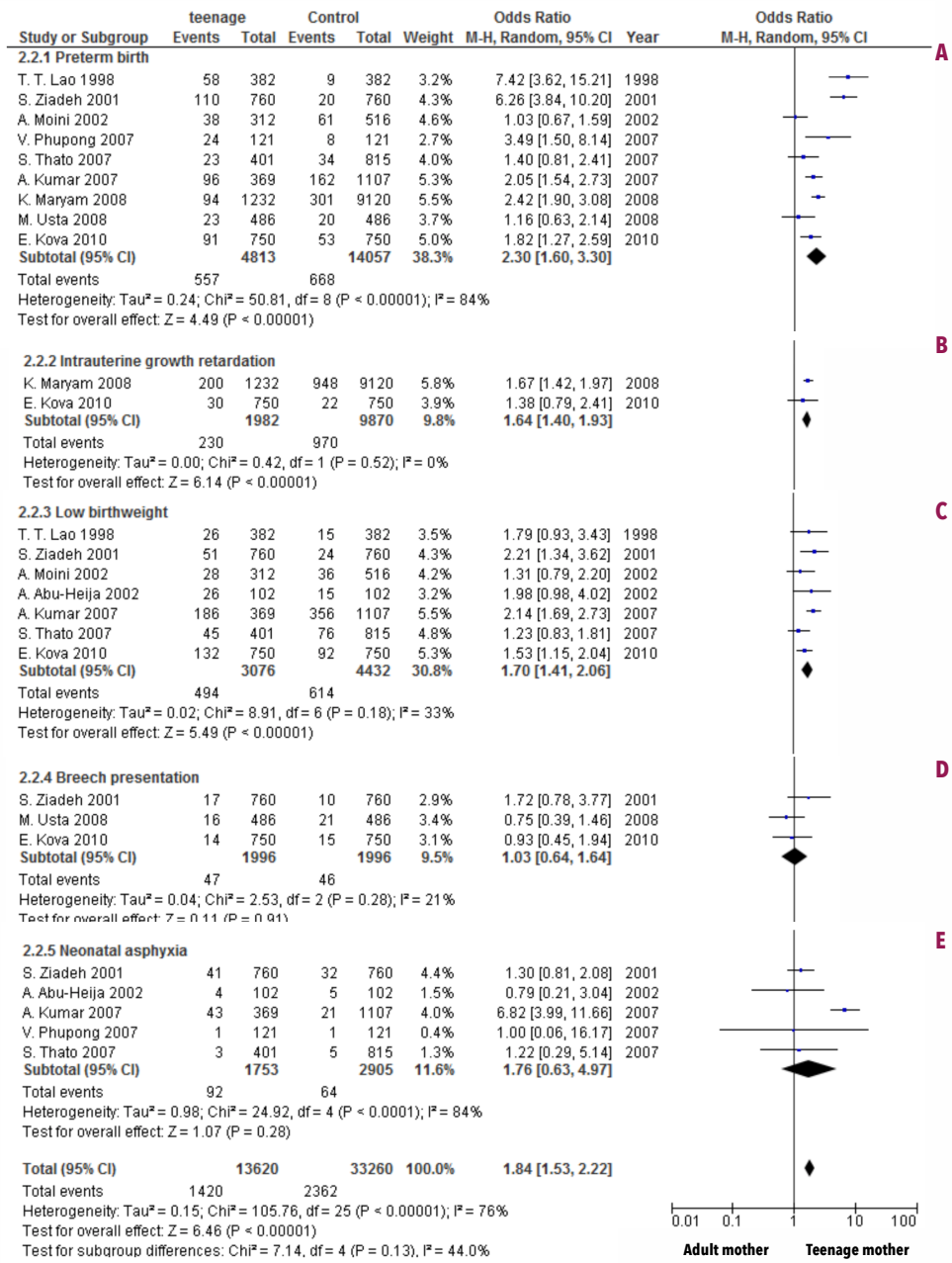

Figure 5. Meta-analysis of the included studies showing secondary outcomes regarding neonatal outcomes of teenage mothers vs. adult mothers.

Neonatal outcomes included Panel A, preterm birth; Panel B, intrauterine growth retardation; Panel C, low birthweight; Panel D, breech presentation and; Panel E, neonatal asphyxia

2,378 adult mothers. We found that the rates of postpartum hemorrhage were similar in both groups (OR, 1.05; 95% CI, 0.73 to 1.52; I^2=0%) (Figure 4, Panel H).

Neonatal outcomes

Preterm birth

Preterm birth was reported in nine eligible studies. Overall, 557 events in 4,813 teenage mothers vs. 668 events in 14,057 adults mothers. We found that preterm birth was significantly more common in teenage mother compared with that of the adult mother (OR, 2.30; 95% CI, 1.60 to 3.30; I^2=84%) (Figure 5, Panel A).

Intrauterine growth retardation

Intrauterine growth retardation was reported in two eligible studies. Overall, 230 events in teenage mothers were reported vs. 970 events in 9,870 adult mothers. We found that intrauterine growth retardation was significantly more common in teenage mother compared with that of the adult mother (OR, 1.64; 95% CI, 1.40 to 1.93; I^2=0%) (Figure 5, Panel B).

Low birth weight

Low birth weight was reported in seven eligible studies. Overall, 494 events in 3,076 teenage mothers were reported vs. 614 events in 4,432 adult mothers. We found that low birth weight was significantly more common in teenage mother compared with that of the adult mother (OR, 1.70; 95% CI, 1.41 to 2.06; I^2=33%) (Figure 5, Panel C).

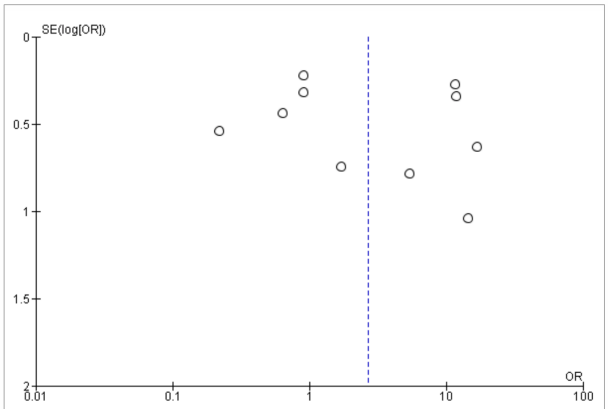

Figure 6. Funnel plot of the primary outcome.

Breech presentation

Breech presentation was reported in three eligible studies. Overall, 47 events in 1,996 teenage mothers were reported vs. 46 in 1,996 adult mothers. We found that the rates of breech presentation were similar in both groups (OR, 1.03; 95% CI, 0.64 to 1.64; I^2=21%) (Figure 5, Panel D).

Neonatal asphyxia

Neonatal asphyxia was reported in five eligible studies. Overall, 92 events in 1,753 teenage mothers were reported vs. 64 in 2,905 adult mothers. We found that the rates of neonatal asphyxia were similar in both groups (OR, 1.76; 95% CI, 0.63 to 4.97; I^2=84%) (Figure 5, Panel E).

PUBLICATION BIAS

We assessed the presence of publication bias by using the funnel plots. The funnel plot was symmetrical, suggested the low chance of publication bias (Figure 6).

SENSITIVITY ANALYSIS

We meta-analyzed two high-quality studies regarding NOS. Overall, 17 events of preeclampsia in 522 teenage mothers were reported vs. 23 events in 936 adult mothers. We found that the rates of preeclampsia were similar in both groups (OR, 1.68; 95% CI, 0.21 to 13.53; I^2=82%).

DISCUSSION

Our meta-analysis included case-control and cohort studies investigating the effect of teenage pregnancy on preeclampsia as well as other maternal and neonatal outcomes in Asian countries. In teenage pregnancy, the meta-analysis demonstrated a significantly increase the risk for preeclampsia. For other maternal outcomes, teenage pregnancy also increased the risk for developing anemia while it decreased the risk for cesarean delivery, gestational diabetes mellitus. For the neonatal outcomes, teenage pregnancy also increased the risk for preterm birth, intrauterine growth retardation and low birthweight. We also did the sub-group analysis by including the studies with high methodological quality only. Preeclampsia was found significantly more common in teenager mother. However, this significance disappeared in the meta-analysis of the high quality studies. Thus, the readers should be cautious when interpreting our findings from all types of study quality.

STRENGTHS AND LIMITATIONS

The findings of the present systematic review are based on the rigorous protocol to identify all possible relevant studies including multiple electronic databases, the tracing for additional studies from the reference lists of the included studies, selecting all studies that met basic entry criteria, strict evaluating methodological quality of the included studies, extracting and analyzing data, and using funnel plot to assess the presence of biases.

However, there were some limitations in the present review that must be considered. First, we excluded non-English studies. This means that potentially relevant articles may not be included. Second, the inclusion of published material causes missing of relevant small studies that tend to be unpublished or studies with non-significant that are frequently delay published. Third, the full-text articles were not all retrievable, thus, missing of relevant data in the meta-analysis is inevitable. Publication bias is a potent threat in our review. It is unlikely to have a major effect in the present study. From the funnel plot, asymmetry was not observed. Still, in the current review, full-text of four potential studies cannot be retrieved, thus, the publication bias might also arise. Fourth, after assessing of methodologic quality, we found that three studies seemed to be cohort studies rather than case-control ones as they were described, therefore, we re-analyzed them as a cohort study. Fifth, only two of 10 studies had high quality (NOS score>5), thus, largely the findings were solely based on relatively poor quality studies. Lastly, our findings had high heterogeneity indicated by the high percentage of I^2 in some outcomes. The conclusion in these outcomes might not be appropriate to be drawn.

COMPARISON WITH OTHER STUDIES

Our review found that teenage pregnancy significantly increased the risk of preeclampsia compared with the adult pregnancy. This corresponds with the previous review published in 2005 that showed a significantly higher rate of preeclampsia in pregnant women aged more than 40 years compared to those with younger maternal age.[30] This might suggest that teenage, as well as elderly pregnancy, have a higher rate of preeclampsia. We found a significant increased in the risk of preterm deliveries, which is similar to the finding of Stevens-Simon et al.[31] Our meta-analysis showed significantly increased risk of low birth weight, however, another study showed variation in the birth weight of infants born to teenage pregnancy.[31]

CONCLUSIONS AND IMPLICATIONS

In conclusion, the reported incidence rate of preeclampsia, anemia and preterm birth for teenage pregnancy are heterogeneous. Much of variability, however, is due to differences in study methodologies that need to be considered when interpreting the data. Moreover, study quality of seems to affect the results of this systematic review. In particular, results from all quality studies showed that teenage pregnancy increased the risk of preeclampsia whereas high-quality studies didn't. The results may be used for observation in all cases of teenage pregnancy for early detection of mentioned complications for prompt treatment. Future study to determine the association between preeclampsia and subgroup of teenage pregnancy such as those extreme young ages (aged younger than 15 years old) should be done.

ACKNOWLEDGMENTS & DECLARATION

The authors would like to thank :Thammasorn Jeeraaumponwat, M.D, Ph.D. for their supervision. We also would like to thank Khon Kaen Medical Education Center, Khon Kaen Hospital for their supports.

COMPETING INTERESTS: This study has no competing on interest.
FUNDING: None

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contact us

www.theclinicalacademia.org

theclinicalacademia@gmail.com

(+66) 095 356 2522

Official LINE: @thaimaf

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-Hannibal Barca

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