

THE CLINICAL ACADEMIA

VOLUME **41** ISSUE **4**
JULY-AUGUST 2017



WE ARE IN Group I of Thai Journal Citation Index (TCI)
ASEAN Citation Index (ACI)

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



the clinical academia

Aim and Scope

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

We.....

- are in ASEAN Citation Index (ACI)
- are in Group I of Thai Journal Citation Index (TCI)
- are open access peer-reviewed journal
- 100% check for plagiarism using "turnitin"
- are a registered member of Committee on Publication Ethics (COPE)
- publish only English articles
- publish every 2 months
- request all submitted manuscripts to be provided to with documents regarding ethical approval
- request all original database to be submitted with every manuscript
- request all submitted randomized controlled trial study to be presented with Clinical Trial Registry Number
- Use Digital Object Identifier System (DOI) for all published documents since 2017

the clinical academia

OWNED BY

The Medical Advancement Foundation

Under the Patronage of

Khon Kaen Medical Education Center
Khon Kaen Hospital
Thai Ministry of Public Health

THE ADVISORY BOARD

Chanchai Janworachaikul, M.D.
Sirijit Vasanawathana, M.D.
Prasit Hanpinitasak, M.D.
Surachai Saranrittichai, M.D.

EDITORIAL BOARD

Professor Tomono Kazunori, Osaka University Hospital, Japan
Associate Professor Hiroshi Nishigori, Kyoto University, Japan
Assistant Professor Lynette J Menezes, University of South Florida, USA
Professor Charurat Somboonwit, dUniversity of South Florida, USA
Professor Nathorn Chaiyakunapruk, Pharm.D., Ph.D., Monash University, Malaysia
Kanokwan Siruksa, M.D., Medical Education Center, Khon Kaen Hospital, Khon Kaen, Thailand

MANAGING EDITOR

Benjaporn Silaruks, B.Pharm., Ph.D. Khon Kaen Hospital, Khon Kaen, Thailand

EDITOR-IN-CHIEF

Thammasorn Jeeraumponwat, M.D., Ph.D.

GRAPHIC ART

Thammasorn Jeeraumponwat, M.D., Ph.D.

Material printed in the *Journal* is covered by copyright. No copyright is claimed to any work of the Thai government. No part of this publication may be reproduced without written permission. The *Journal* does not hold itself responsible for statements made by any contributors. Statements or opinions express in the *Journal* reflect the views of the author(s) and do not represent the official policy of the *Journal* unless stated.

message from the editor

In the era of social media, sharing is inevitable. But the content of what you share is not always fact. Information is plenty where wisdom is scarce. The Clinical Academia together with Medical Advancement Foundation has initiated the Official Line account, facebook fanpage, Instagram, Twitter to communicate with the world. We try to disseminate trending information in the field of medicine. Follow us via the given information below.

Twitter: @thai_maf

Instagram: @thaimaf

Facebook Fanpage: Thai Maf

Line Official: @thaimaf

The world of medicine is ever changing. Here now and then are its places. Keep going is the best suggestion for all of us. Hope you enjoy reading The Clinical Academia.

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

submission

Please visit

www.theclinicalacademia.org

For online submission

*Our issues of each volume will be published online
on
1st of February, April, June, August, October and December*

reviewing process

All accepted articles are classified into two main categories;

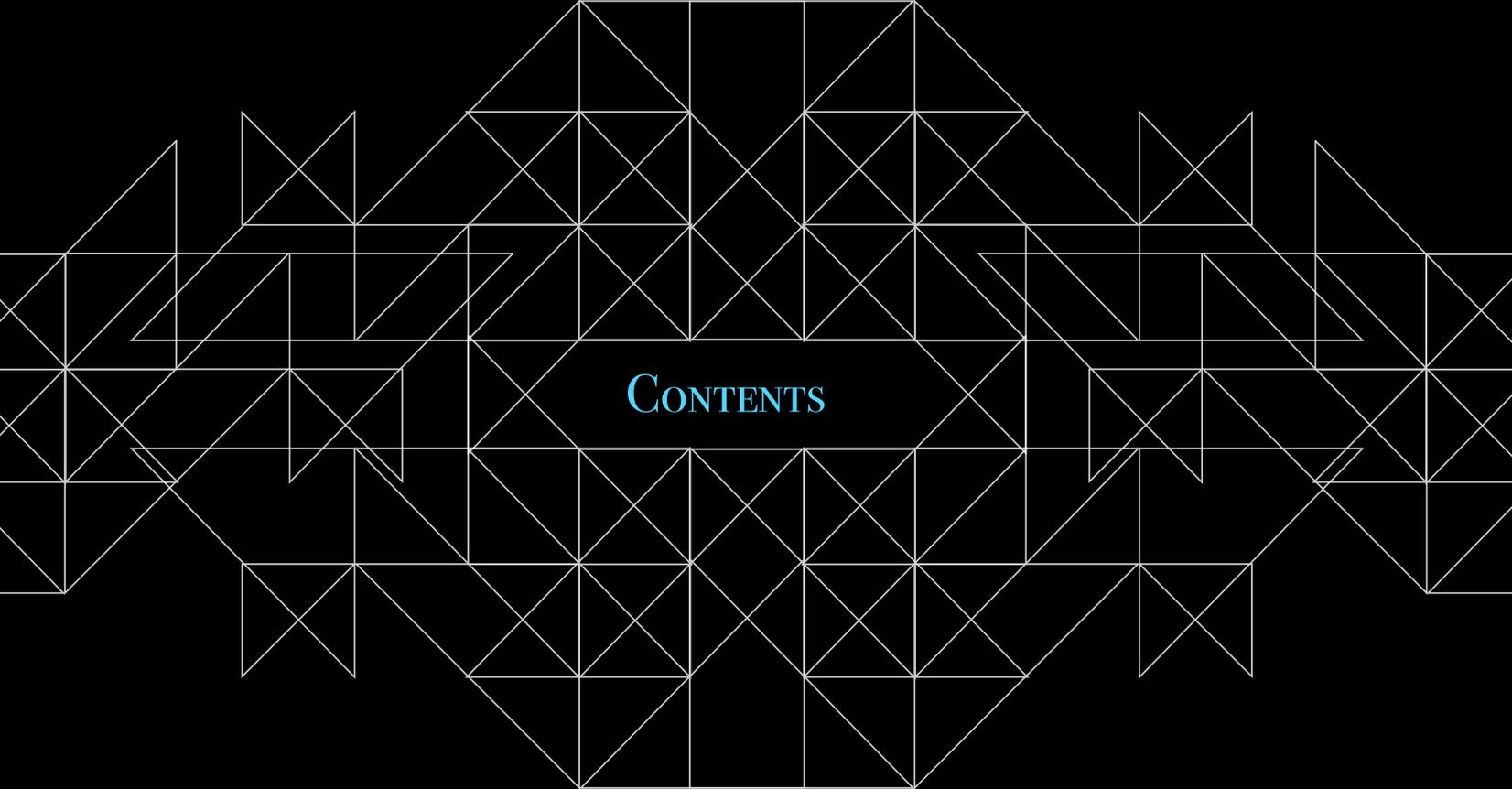
"**standard submission**" with the approximated processing time of 3-4 months and
"**expression submission**" with the approximated processing time of 1-2 months. For the
latter category, the author must submit as standard submission with notifying our journal
for express submission.

Email: theclinicalacademia@gmail.com

Telephone: (+66) 093 624 4422

Official LINE: @thaimaf





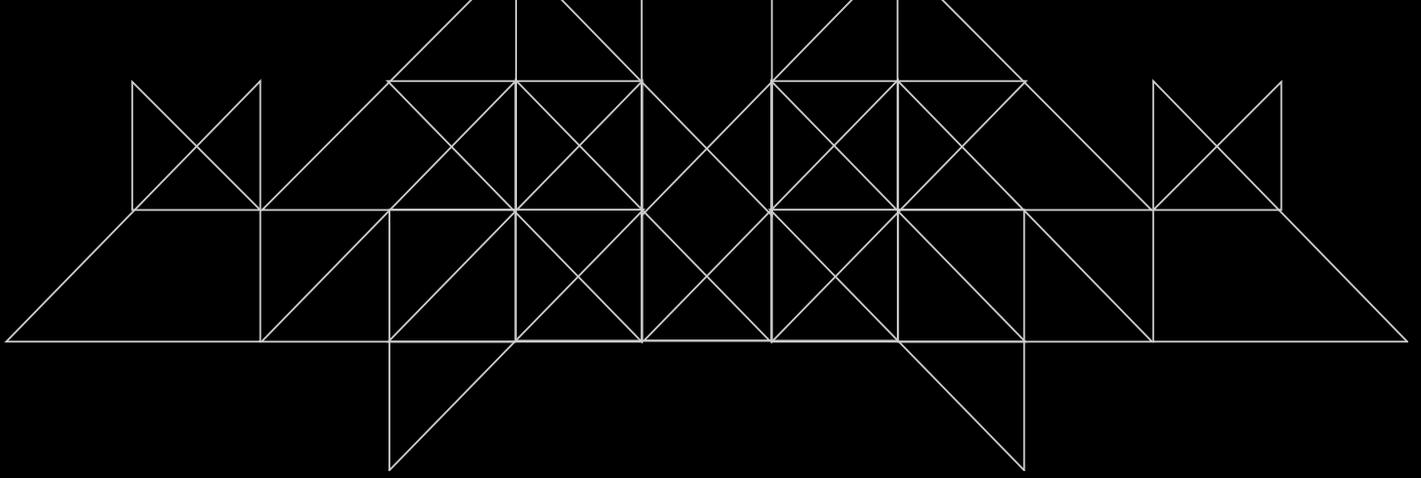
CONTENTS

International Committee of Medical Journal Editors (ICMJE) Recommendation for
Preparing for Submission

viii

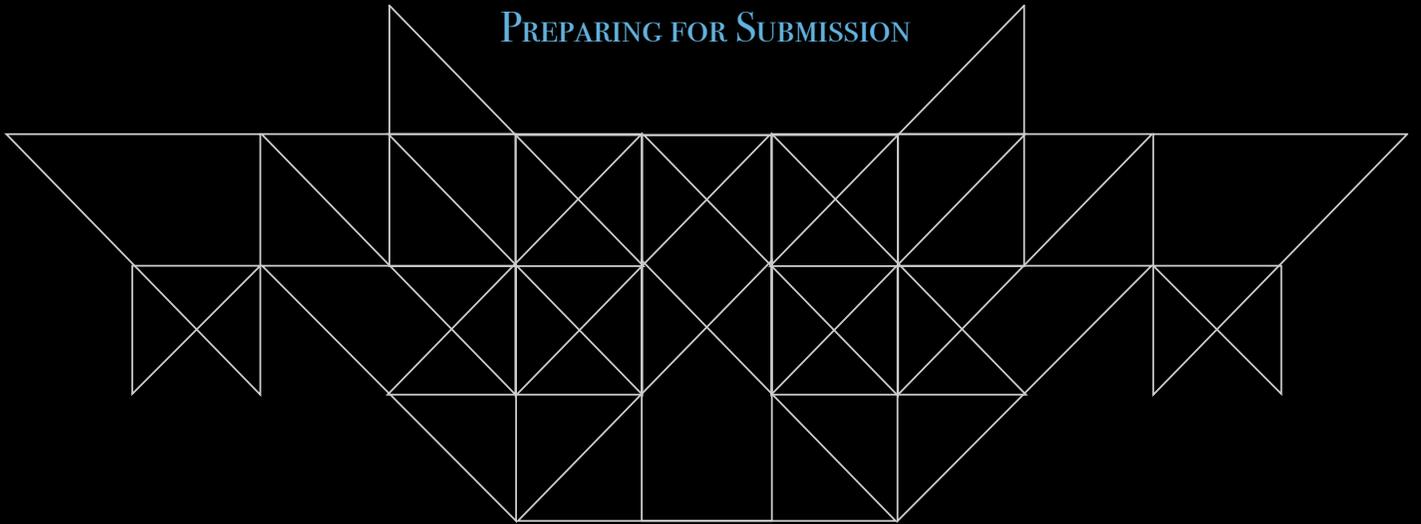
Original Articles

- *Diabetes and acute pancreatitis after endoscopic retrograde
cholangiopancreatography* 122
- *APACHE II Score for predicting of ventilator-associated pneumonia in intensive care
unit* 131
- *Birth asphyxia in teenage pregnancy* 142



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, selecting, 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 findings 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.

If you use data from another published or unpublished source, obtain permission and acknowledge that source fully.

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.

Diabetes and acute pancreatitis after endoscopic retrograde cholangiopancreatography

ORIGINAL ARTICLE BY

Atitaya Sakunthai¹, M.D.; Nitikul Chitpreeda², M.D.; Theerakarn Charoenchai³, M.D.; Worakanya Thongnuch⁴, M.D.

¹Nong Rua Hospital, Thailand; ²Phra Ajarn Fun Arjaro Hospital, Thailand; ³Waeng Noi Hospital, Thailand, ⁴Prasat Neurological Hospital and Institute, Thailand

Accepted: April 2017
Latest revision: May 2017
Printed: June 2017

Correspondence to: Atitaya Sakunthai
a.sakunthai@gmail.com

ABSTRACT

OBJECTIVE

To identify the association between diabetes and acute pancreatitis after endoscopic retrograde cholangiopancreatography (ERCP)

METHODS

This was a retrospective cohort study using and reviewing the medical record of patients undergoing ERCP at Khon Kaen Hospital between April 2009 and March 2014. We assessed the risk of pancreatitis as our primary outcome linked to diabetes as our exposure of interest.

RESULTS

A total of 1,644 patients, 1,434 patients were included in our analysis. There are 230 patients with diabetes (16.0%). The most common complication of ERCP was acute pancreatitis that occurred in 13 patients with diabetes (5.7%) as compared with 82 patients (6.8%) in the nondiabetes patients. (adjusted odds ratio (AOR), 0.79; 95% confidence interval (CI) 0.41 to 1.52). From binary logistic regression analysis, we found that age over 59 years old was the protective factor for developing post ERCP pancreatitis (AOR, 0.61; 95% CI 0.38 to 0.98) but sphincterotomy was the risk factor for developing post ERCP pancreatitis (AOR, 2.36; 95% CI 1.24 to 4.51). Risk factors of acute cholangitis after ERCP were ALP > 246 U/L (AOR, 1.84; 95% CI 1.01 to 3.34) and insertion of stent into bile duct (AOR, 2.09; 95% CI 1.17 to 3.75), but the protective factors for developing cholangitis was sphincterotomy and papillotomy (AOR, 0.50; 95% CI 0.28 to 0.89). In relation to sepsis, creatinine level over 2 mg/dl was the risk factor for developing sepsis (AOR, 2.66; 95% CI 1.02 to 6.94) but stone extraction was the protective factor (AOR, 0.35; 95% CI 0.14 to 0.84).

CONCLUSION

No association between diabetes and acute pancreatitis in those undergoing ERCP was found.

INTRODUCTION

Endoscopic retrograde cholangiopancreatography (ERCP) is one of the most common endoscopic procedures.¹ It has been used for both diagnosis and treatment for a variety of disorders including diagnosis and management biliary perioperative complications and pancreatic tumor.²⁻⁴ However, it also causes a relatively high complication rate; nearly half of the patients experienced complications including pancreatitis, cholangitis, retroperitoneal perforation, and hemorrhage.⁵⁻¹¹ From a previous study, sphincterotomy, sphincter of Oddi dysfunction, younger age, female sex, past history of pancreatitis, pancreas divisum, the difficulty of cannulation and primary sclerosing cholangitis were factors found to be associated with the higher rate of post-ERCP pancreatitis and cholangitis.¹² For diabetes, the prior study demonstrated that diabetic patients had more frequent postoperative complications and higher mortality rate compared to those without diabetes. Moreover, early studies implicated diabetes as a risk factor for serious postoperative complications. However, many of these conclusions have not withstood the scrutiny of analyses correcting for comorbid conditions.¹³ Therefore, our study was designed to examine the association between diabetes and pancreatitis as well as other complications in patients underwent ERCP.

METHODS

STUDY DESIGN AND PARTICIPANTS

We conducted a retrospective cohort study by reviewing medical records of patients who

underwent ERCP at Khon Kaen Hospital between April 2009 and March 2014 to assess whether diabetes was a risk factor for pancreatitis after ERCP. To determine this relationship, with 80% power, 5% alpha error, we required 15,202 patients in total.

DATA COLLECTION

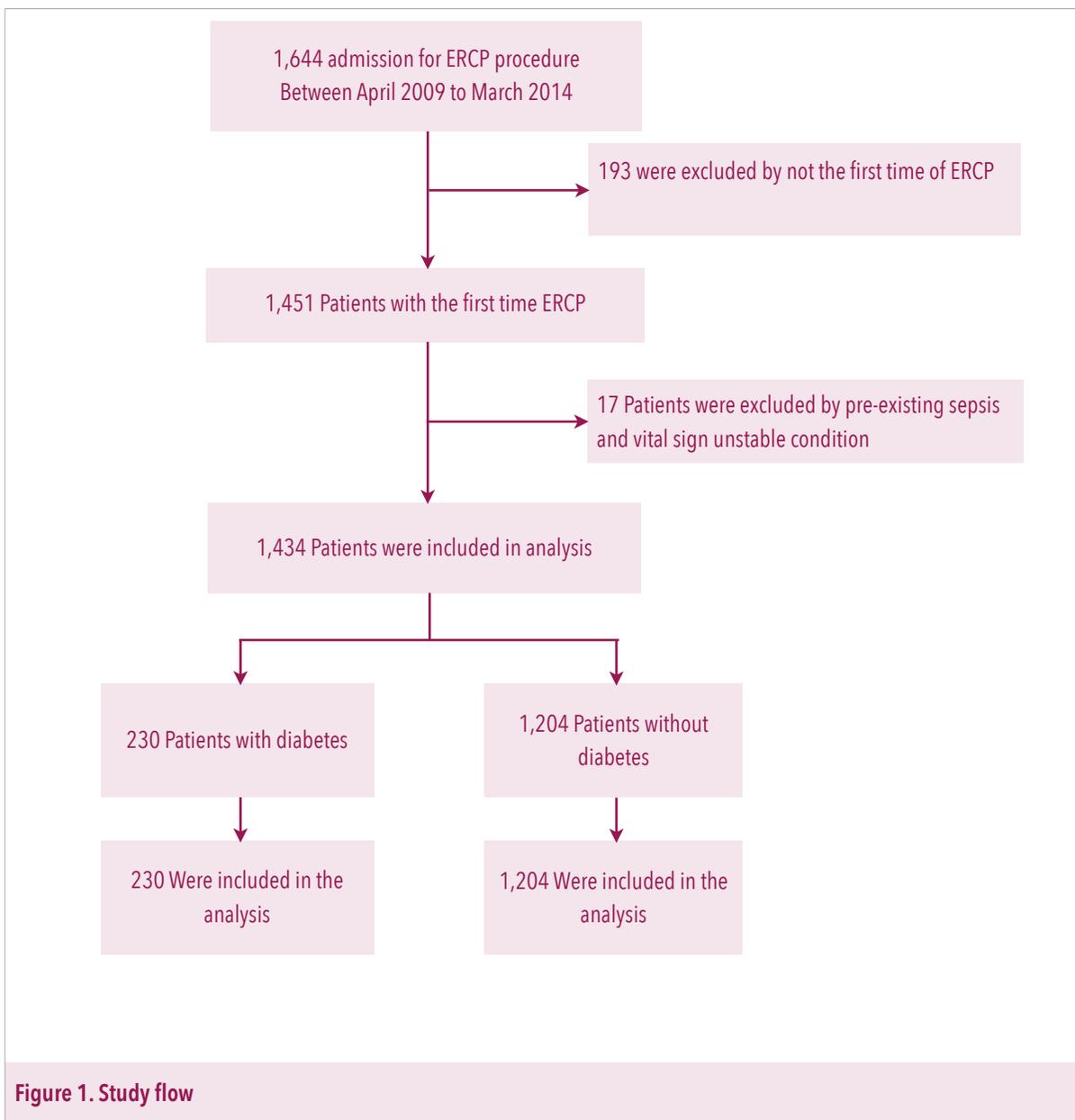
From data reviewing, variables including gender, age, indication for ERCP, procedure, complication after the ERCP were verified and collected onto spreadsheet with double entry technique. We included only patients who do the first time of ERCP. We excluded those with pre-existing sepsis or with the unstable vital signs.

STUDY OUTCOMES

The primary outcome of the study was any severity of the post ERCP pancreatitis within the same hospital admission. We diagnosed the post ERCP pancreatitis from the clinical of the patient (acute abdominal pain and tenderness) and laboratory finding (serum amylase > 316 U/L)¹⁴. Secondary outcomes included age, sex, underlying diseases, the procedure during ERCP related post-ERCP complications.

STATISTICAL ANALYSIS

All data were clean before analysis. For descriptive statistics, categorical variables were summarized using number and percentage while normally distributed continuous variables were summarized using mean and standard deviation (SD) and non-normally distributed continuous variables were present using median and interquartile range (IQR).



For validity of the model predicting outcomes in the present study, it was interpreted regarding sensitivity, specificity, positive likelihood ratio (LR) and receiver operating characteristic (ROC) curve together with their 95% confidence interval (CI).

RESULTS

CHARACTERISTICS OF THE PATIENTS

In the present study, 1,644 records were reviewed (Figure 1). However, only 1,434 were left in the analysis. In general, most of them were male

Table 1. Pretreatment Characteristics of the Patients.

Characteristic	Diabetes	Non-diabetes	P Value
Male sex–no. (%)	87 (37.8)	695 (57.7)	<0.001
Age–yr			<0.022
Median	67	65	
Interquartile range	60-74	55-73	
Indications for ERCP–no. (%)			
Choledocholithiasis	102 (44.3)	543 (45.1)	0.834
Biliary and pancreatic neoplasms	63 (27.4)	326 (27.1)	0.922
Common bile duct stenosis	12 (5.2)	15 (1.2)	<0.001
Intrahepatic duct stone	0	4 (0.3)	1
Pancreatic stone	1 (0.4)	2 (0.2)	0.408
Common bile duct obstruction	44 (19.1)	266 (22.1)	0.317
Other biliary tract diseases	8 (3.5)	65 (5.4)	0.225
Diagnosed chronic conditions–no. (%)			
Hypertension	107 (46.5)	137 (11.4)	<0.001
Dyslipidemia	16 (7.0)	15 (1.2)	<0.001
Heart disease	10 (4.3)	21 (1.7)	0.022
Psychiatric, emotional, or nervous condition	0	6 (0.5)	0.598
Preoperative laboratory			
Hematocrit–%			0.001
Median	32 (224/230)	33.4 (1180/1204)	
Interquartile range	28.9-35.5	29.7-37.2	
Platelet count–103/ml			0.971
Median	288.5 (224/230)	291 (1179/1204)	
Interquartile range	229.5-384	224-376	
Creatinine–mg/dl			0.056
Median	0.9 (226/230)	0.9 (1179/1204)	
Interquartile range	0.7-1.2	0.7-1.1	
Aspartate aminotransferase–U/L			0.724
Median	66.5 (224/230)	61 (1167/1204)	

Table 1. (Continued)

Characteristic	ARM (n=510)	SRM (n=491)	P Value
Interquartile range	33-114.8	33-115	
Alanine aminotransferase-U/L			0.674
Median	50 (223/230)	51 (1166/1204)	
Interquartile range	27-87	29.0-92.3	
Alkaline phosphatase-U/L			0.017
Median	281(223/230)	229.5 (1170/1204)	
Interquartile range	135-542	112-449	

(54.5%) with the median age of 65 years old. The most common indication for ERCP was choledocholithiasis (45.0%). Hypertension was the most common chronic condition found in our patients (17.0%).

Comparing between diabetes group and nondiabetes group, the former were slightly older ($P=0.022$) with the higher proportion of female ($P<0.001$) and they also have higher proportion of those with hypertension, dyslipidemia and heart diseases as well as the common bile duct stenosis ($P<0.001$, $P<0.001$, $P=0.022$ and $P<0.001$, respectively)(Table 1). Regarding laboratory test, hematocrit in the former was slightly lower ($P=0.001$) while alkaline phosphatase tended to be higher ($P=0.017$). However, the other characteristics and laboratory tests were no differences between the two groups.

TREATMENT OUTCOMES

The overall post ERCP pancreatitis occurred in 13 patients with diabetes (5.7%) as compared with 82 patients (6.8%) in the nondiabetes (RR, 0.83; 95% CI 0.47 to 1.46) (Table 2). Several complications of

patients who underwent ERCP are presented in Table 2. Acute cholangitis occurred in 7 patients of diabetes (3.0%) and 59 patients of nondiabetes (4.9%) (RR, 0.62; 95% CI, 0.29 to 1.34). Sepsis occurred in 5 patients of diabetes (2.2%) versus 42 patients (3.5%) of nondiabetes (RR, 0.62; 95% CI 0.25 to 1.56), and 1 diabetic patient died (0.4%) compared with 8 patients of nondiabetes (0.7%) (RR, 0.65; 95% CI 0.08 to 5.21). Moreover, 2 complications that not found in diabetic patients were hemorrhage and perforation. However, two patients (0.2%) with nondiabetes had the hemorrhagic complication and nine patients (0.7%) had perforations of biliary tract and gastrointestinal tract. There was no significant difference of incident rate of acute pancreatitis and other complications between those with diabetes and nondiabetes.

From binary logistic regression analysis, sphincterotomy was the risk factor for developing acute pancreatitis (COR, 2.08; 95% CI 1.18 to 3.66, AOR, 2.36; 95% CI 1.24 to 4.51)(Table 3). but age over 59 years old was the protective factor for developing acute pancreatitis (AOR, 0.61; 95% CI

Table 2. Post ERCP Complication.

Complication	Diabetes	Non-diabetes	Relative risk (95% CI)
Acute pancreatitis–no. (%)	13 (5.7)	82 (6.8)	0.83 (0.47-1.46)
Acute cholangitis–no. (%)	7 (3.0)	59 (4.9)	0.62 (0.29-1.34)
Sepsis–no. (%)	5 (2.2)	42 (3.5)	0.62 (0.25-1.56)
Deaths–no. (%)	1 (0.4)	8 (0.7)	0.65 (0.08-5.21)

0.38 to 0.98). However, male sex, hematocrit, creatinine level over 2 mg/dl, diabetes, hypertension, insertion of the bile duct, dilatation of bile duct and stone extraction were not found to be associated with acute pancreatitis. For acute cholangitis, there were 2 risk factors associated with acute cholangitis after ERCP; ALP>246 U/L (COR, 2.65; 95% CI 1.54 to 4.56, AOR, 1.84; 95%CI 1.01 to 3.34) and insertion of stent into bile duct (COR, 2.66; 95% CI 1.62 to 4.38, AOR, 2.09; 95%CI 1.17 to 3.75), but the protective factors for developing cholangitis was sphincterotomy and papillotomy (COR, 0.60; 95% CI 3.36 to 1.00, AOR, 0.50; 95%CI 0.28 to 0.89). In relation to sepsis, creatinine level over 2 mg/dl was the risk factor for developing sepsis (COR, 3.83; 95% CI 1.55 to 9.44, AOR, 2.66; 95% CI 1.02 to 6.94) but stone extraction was the protective factor (COR, 0.30; 95% CI 0.13 to 0.67, AOR, 0.35; 95% CI 0.14 to 0.84) while other factors we did not found the relationship to sepsis. In addition to this, there seemed to be no factors associated with mortality of the patients after ERCP.

DISCUSSION

MAIN FINDINGS

In this retrospective cohort, we found that the

incidence of post ERCP pancreatitis in patients with diabetes was not significantly different from that of those without diabetes. The incidence of acute pancreatitis increased with sphincterotomy and decreased with age older than 59 years old. Moreover, serum ALP elevated more than 246 U/L increased the incidence of acute cholangitis, but sphincterotomy and stone extraction reduced the incidence of acute cholangitis and sepsis, respectively. Additionally, serum creatinine elevated more than 2 mg/dl was a risk factor for sepsis after ERCP. Finally, we found no factors associated with acute pancreatitis after ERCP.

COMPARISON WITH OTHER STUDIES

In the present study, we found that diabetes was not associated with any post-ERCP complications. This supported the previous study observed that diabetes did not increase the risk for mortality in biliary tract procedure.¹⁶ One prior study stated that creatinine level over 2 mg/dl was the risk factor for post-ERCP pancreatitis.¹⁷ However, our study suggested no association between the creatinine level more than 2 mg/dl and pancreatitis. This differences might be due to patients' status were not similar.

We found sphincterotomy of bile duct was the risk factor of post-ERCP pancreatitis. This was

Table 3. Factors Related with Post ERCP Complications.

Factor	Acute pancreatitis		Acute cholangitis		Sepsis		Death	
	COR (95% CI)	AOR (95% CI)	COR (95% CI)	AOR (95% CI)	COR (95% CI)	AOR (95% CI)	COR (95% CI)	AOR (95% CI)
Age > 59 yr	0.72 (0.47-1.11)	0.61(0.38-0.98))	0.94 (0.55-1.61)	0.91 (0.52-1.60)	0.97 (0.51-1.82)	0.94 (0.48-1.84)	1.44 (0.30-6.95)	1.70 (0.33-8.66)
Male sex	0.77 (0.51-1.17)	0.90 (0.57-1.40)	1.59 (0.95-2.67)	1.36 (0.79-2.33)	1.24 (0.68-2.24)	1.06 (0.57-1.97)	2.94 (0.61-14.18)	2.21 (0.44-11.14)
Hematocrit (%)	1.02 (0.98-1.06)	1.00 (0.95-1.04)	0.94 (0.90-0.99)	0.98 (0.93-1.03)	0.92 (0.87-0.97)	0.94 (0.88-1.00)	1.00 (0.88-1.14)	1.04 (0.91-1.20)
Creatinine > 2 mg/dl	0.52 (0.13-2.19)	0.56 (0.13-2.40)	1.16 (0.35-3.80)	0.88 (0.26-3.02)	3.83 (1.55-9.44)	2.66 (1.02-6.94)	N/A	N/A
ALP > 246 U/L	0.62 (0.40-0.96)	0.63 (0.39-1.04)	2.65 (1.54-4.56)	1.84 (1.01-3.34)	1.68 (0.92-3.05)	1.34 (0.69-2.59)	3.61 (0.75-17.45)	4.10 (0.77-21.92)
Diabetes	0.82 (0.45-1.50)	0.79 (0.41-1.52)	0.61 (0.28-1.35)	0.61 (0.26-1.42)	0.62 (0.24-1.57)	0.53 (0.19-1.45)	0.65 (0.08-5.25)	0.84 (0.09-7.66)
Hypertension	1.42 (0.86-2.35)	1.74 (0.98-3.11)	0.66 (0.31-1.40)	1.01 (0.45-2.27)	1.00 (0.46-2.17)	0.24 (0.53-2.89)	0.61 (0.08-4.88)	0.70 (0.08-6.38)
Insertion of stent into bile duct	0.97 (0.62-1.52)	0.93 (0.54-1.58)	2.66 (1.62-4.38)	2.09 (1.17-3.75)	0.99 (0.53-1.85)	0.68 (0.33-1.43)	0.60 (0.12-2.91)	0.49 (0.82-2.92)
Sphincterotomy	2.08 (1.18-3.66)	2.36 (1.24-4.51)	0.60 (0.36-1.00)	0.50 (0.28-0.89)	0.65 (0.35-1.20)	1.09 (0.55-2.19)	0.47 (0.13-1.75)	0.68 (0.15-3.14)
Dilatation of bile duct	1.48 (0.97-2.24)	1.45 (0.91-2.33)	1.47 (0.90-2.42)	1.46 (0.82-2.61)	0.66 (0.34-1.25)	0.78 (0.37-1.65)	0.49 (0.10-2.39)	0.68 (0.12- 4.05)
Stone extraction	0.88 (0.57-1.37)	0.63 (0.37-1.06)	0.46 (0.25-0.83)	0.77 (0.40-1.50)	0.30 (0.13-0.67)	0.35 (0.14-0.84)	0.50 (0.10-2.40)	0.61 (0.10-3.63)

N/A=not applicable

supported by many studies.^{6,18,19,20} However, one study demonstrated sphincterotomy and papillotomy as a precut technique reduced the risk of pancreatitis after ERCP.²¹ The contrary outcome might be from our sphincterotomy and papillotomy was done by standard attempt but the prior study was done as a precut technique for cannulation. In addition to this, age over 59 years old was the protective factor for pancreatitis after ERCP and the previous study was also supported

these findings.⁶ For post-ERCP cholangitis, sphincterotomy and insertion of stent into bile duct is a risk factor whether we reviewed the study and also found the same outcome that further supported ours.^{22,23,24}

LIMITATION OF THE STUDY

This study has several limitations. Firstly, we were not able to assess the severity of each comorbidity of the patients due to many patients did not follow

up the diseases with us that may affect to complications such as diabetes that we cannot know whether they had any microvascular or macrovascular complications yet. Secondly, time to the event of the outcome was not recorded. Thirdly the sample size of this study was not adequate to detect 1.1% difference given the type 1 error of 5% and power of 80%. We required as many as 15,202 patients in two groups. However, we had 1,434 patients included in the present study.

CONCLUSION AND IMPLICATION

The results from our study indicate that no association between diabetes and pancreatitis after ERCP. To determine the association more precisely between diabetes and post ERCP pancreatitis, the further study needs a larger prospective cohort study as well as the information regarding the severity of diabetes such as HbA1C level to get an overall picture of their average blood sugar controlled.

ACKNOWLEDGMENTS & DECLARATION

The authors would like to thank :Thammasorn Jeeraumponwat, 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

REFERENCES

1. Maple JT, Ben-Menachem T, Anderson MA, et al. The role of endoscopy in the evaluation of suspected choledocholithiasis. *Gastrointest Endosc* 2010;71:1-9
2. Maple JT, Ben-Menachem T, Anderson MA, et al. The role of endoscopy in the evaluation of suspected choledocholithiasis. *Gastrointest Endosc* 2010;71:1-9.
3. Baron TH, Mallery JS, Hirota WK, et al. The role of endoscopy in the evaluation and treatment of patients with pancreaticobiliary malignancy. *Gastrointest Endosc* 2003;58:643-9.
4. Costamagna G, Shah SK, Tringali A. Current management of postoperative complications and benign biliary strictures. *Gastrointest Endosc Clin N Am* 2003;13:635-48, ix.
5. Vandervoort J, Soetikno RM, Tham TC, Wong RC, Ferrari AP, Jr, Montes H, Roston AD, Slivka A, Lichtenstein DR, Ruymann FW, Dam J, Hughes M, Carr-Locke DL. Risk factors for complications after performance of ERCP. *Gastrointest Endosc*. 2002;56:652-656. doi: 10.1016/S0016-5107(02)70112-0. [PubMed] [Cross Ref]
6. Mehta SN, Pavone E, Barkun JS, Bouchard S, Barkun AN. Predictors of post-ERCP complications in patients with suspected choledocholithiasis. *Endoscopy*. 1998;30:457-463. doi: 10.1055/s-2007-1001308. [PubMed] [Cross Ref]
7. Cheng CL, Sherman S, Watkins JL, Barnett J, Freeman M, Geenen J, Ryan M, Parker H, Frakes JT, Fogel EL, Silverman WB, Dua KS, Aliperti G, Yakshe P, Uzer M, Jones W, Goff J, Lazzell-Pannell L, Rashdan A, Temkit M, Lehman GA. Risk factors for post-ERCP pancreatitis: a prospective multicenter study. *Am J Gastroenterol*. 2006;101:139-147. doi: 10.1111/j.1572-0241.2006.00380.x. [PubMed] [Cross Ref]
8. Rabenstein T, Schneider HT, Bulling D, Nicklas M, Katalinic A, Hahn EG, Martus P, Ell C. Analysis of the risk factors associated with endoscopic sphincterotomy techniques: preliminary results of a prospective study, with emphasis on the reduced risk of acute pancreatitis with low-dose anticoagulation treatment. *Endoscopy*. 2000;32:10-19. doi: 10.1055/s-2000-138. [PubMed] [Cross Ref]

9. Christoforidis E, Goulimaris I, Kanellos I, Tsalis K, Demetriades C, Betsis D. Post-ERCP pancreatitis and hyperamylasemia: patient-related and operative risk factors. *Endoscopy*. 2002;34:286-292. doi: 10.1055/s-2002-23630. [PubMed] [Cross Ref]
10. Williams EJ, Taylor S, Fairclough P, Hamlyn A, Logan RF, Martin D, Riley SA, Veitch P, Wilkinson ML, Williamson PR, Lombard M. Risk factors for complication following ERCP: results of a large-scale, prospective multicenter study. *Endoscopy*. 2007;39:793-801. doi: 10.1055/s-2007-966723. [PubMed][Cross Ref]
11. Freeman ML. Adverse outcomes of ERCP. *Gastrointest Endosc*. 2002;56:S273-S282. doi: 10.1016/S0016-5107(02)70025-4. [PubMed][Cross Ref]
12. Jeurnink SM, Siersema PD, Steyerberg EW, Dees J, Poley JW, Haringsma J, et al. Predictors of complications after endoscopic retrograde cholangiopancreatography: a prognostic model for early discharge. *Surg Endosc*. 2011 Sep;25(9):2892-900
13. Babineau TJ, Bothe A Jr. General surgery considerations in the diabetic patient. *Infect Dis Clin North Am*. March 1995;9(1):183-93.
14. Kiriya S, Gabata T, Takada T, Hirata K, Yoshida M, Mayumi T, et al. New diagnostic criteria of acute pancreatitis. *J Hepatobiliary Pancreat Sci*. 2010 Jan 1;17(1):24-36.
15. Mehta SN, Pavone E, Barkun JS, Bouchard S, Barkun AN. Predictors of post-ERCP complications in patients with suspected choledocholithiasis. *Endoscopy*. 1998 Jun;30(5):4
16. Sandler RS, Maule WF, Baltus ME. Factors associated with postoperative complications in diabetics after biliary tract surgery. *Gastroenterology*. July 1986;91(1): 157-62.
17. Balderramo D, Bordas JM, Sendino O, Abalde JG, Navasa M, Llach J, et al. Complications after ERCP in liver transplant recipients. *Gastrointestinal Endoscopy*. 2011 Aug;74(2):285-94.
18. Coté GA, Sagi SV, Schmidt SE, Lehman GA, McHenry L, Fogel E, et al. Early measures of hemoconcentration and inflammation are predictive of prolonged hospitalization from post- endoscopic retrograde cholangiopancreatography pancreatitis. *Pancreas*. 2013 Jul;42(5):850-4.
19. Huibregtse K. Complications of Endoscopic Sphincterotomy and Their Prevention. *New England Journal of Medicine*. 1996;335(13):961-3.
20. Freeman ML, Nelson DB, Sherman S, Haber GB, Herman ME, Dorsher PJ, et al. Complications of Endoscopic Biliary Sphincterotomy. *New England Journal of Medicine*. 1996;335(13):909-19.
21. Information NC for B, Pike USNL of M 8600 R, MD B, Usa 20894. Can early precut implementation reduce endoscopic retrograde cholangiopancreatography-related complication risk? Meta-analysis of randomized controlled trials [Internet]. PubMed Health. 2010 [cited 2014 Apr 28].
22. Ertuğrul I, Yüksel I, Parlak E, Çiçek B, Ataseven H, Başar O, et al. Risk factors for endoscopic retrograde cholangiopancreatography-related cholangitis: a prospective study. *Turk J Gastroenterol*. 2009 Jun;20(2):116-21.
23. Zhou H, Li L, Zhu F, Luo S-Z, Cai X-B, Wan X-J. Endoscopic sphincterotomy associated cholangitis in patients receiving proximal biliary self-expanding metal stents. *HBPD INT*. 2012 Dec 15;11(6):643-9.
24. Liguory C, Lefebvre JF, Bonnel D. [Endoscopic retrograde cholangiopancreatography and biliary prosthesis]. *Rev Prat*. 1991 Jan 21;41(3): 220-4.
25. Sripan B, Pairojkul C. Cholangiocarcinoma: lessons from Thailand. *Curr Opin Gastroenterol*. 2008 May;24(3):349-56.
26. Andriulli A, Loperfido S, Napolitano G, Niro G, Valvano MR, Spirito F, et al. Incidence rates of post-ERCP complications: a systematic survey of prospective studies. *Am J Gastroenterol*. 2007 Aug;102(8):1781-8.

APACHE II Score for predicting of ventilator-associated pneumonia in intensive care unit

ORIGINAL ARTICLE BY

Chaisiri Burinkul¹, M.D.; Korawich Karnprakobdee², M.D.;
Paranee Srisupa³, M.D.; Wilasinee Phitsanu⁴, M.D.

¹Nong Na Kham Hospital Thailand; ²Ban Phai Hospital, Thailand; ³Tha Uthen Hospital, Thailand, ⁴Thammasat Chalermprakiet Hospital, Thailand

Accepted: April 2017
Latest revision: May 2017
Printed: August 2017

Correspondence to: Chaisiri Burinkul;
c.burinkul@gmail.com

ABSTRACT

OBJECTIVE

To identify the association between APACHE II score and ventilator-associated pneumonia.

METHODS

We performed a retrospective cohort designed to detect a risk of VAP related to APACHE II score, excluding patients with previous pneumonia, admitted more than one times, admitted to the ICU for less than 48 hours or without complete data records. The cohort included patients aged above 20 years who hospitalized in the ICU at Khon Kaen Hospital between March 2009 and March 2014 with a total of 1,048 patients.

RESULTS

APACHE II score did not increase the risk of VAP (adjusted odds ratio [AOR], 0.98; 95% confidence interval [CI], 0.94 to 1.01). From binary logistic regression analysis we found that history of prior prescribed with cephalosporin was the protective factor for developing VAP (AOR, 0.59; 95% CI 0.40 to 0.86) but the risk factor of developing VAP were tracheostomy (AOR, 1.86; 95% CI 1.02 to 3.40), endotracheal intubation (AOR, 2.42; 95% CI 1.24 to 4.73), post operation (AOR, 1.50; 95% CI 1.06 to 2.12) and hospitalization longer than 5 days (AOR, 3.48; 95% CI 2.30 to 4.98). Our study also showed no significant association between APACHE II score and death.

CONCLUSION

This study showed no evidence that APACHE II score more than 20 was associated with an increased risk of ventilator-associated pneumonia.

INTRODUCTION

Ventilator-associated pneumonia (VAP) is found about 20% of patients on mechanical ventilation.¹ It is a serious complication that can lengthen hospital stay in the intensive care unit (ICU).² It is also the most common nosocomial infection with high mortality rate especially those admitted to the ICU.³ In the ICU, APACHE II score consisting of 12 clinical measurements that are obtained within 24 hours after admission to the ICU was used to triage the treatment and prognosis of the patients.⁴ Many studies state that high APACHE II score is associated with nosocomial infections.⁵⁻⁸ Nevertheless, a previous prospective cohort study found no association between APACHE II and nosocomial infection risk.⁹ Moreover, a study in 113 trauma patients, also suggested that APACHE II score even decreased risk for the development of nosocomial infection.¹⁰ Thus, the association between APACHE II score and nosocomial infection is still controversial. The association between APACHE II score and VAP also has never been well identified as well as its prognostic property for diagnosis VAP. Thus, in the current study, we aimed to assess the association between APACHE II score and VAP and evaluate the prognostic property of APACHE II score for VAP diagnosis.

METHODS

STUDY DESIGN

We designed the current study as a retrospective cohort to assess the association between APACHE II score and VAP. In the later stage, we conducted a

diagnostic study to examine the diagnostic property of APACHE II score for diagnosis of VAP.

PATIENTS

The patients included in the presented study were those admitted to the ICU, Khon Kaen Hospital, Thailand between March 2009 and March 2014. Patients were aged 20 years or older and they were excluded if they had one or more of the following findings: previous pneumonia, admitted more than one times, admitted to the ICU for less than 48 hours, incomplete records of APACHE II score.

EXPOSURE

Factors that might associate with VAP were reviewed from the patient medical records and were collected onto the spreadsheet. This included age¹², male¹², smoking¹³, congestive heart failure¹⁴, diabetes mellitus¹⁴, chronic obstructive pulmonary disease^{14,15}, chronic liver disease¹³, prior third-generation cephalosporin usage¹⁵, head trauma¹³, tuberculosis, post-operation, severe organ insufficiency or immunocompromised, hospitalization more than 5 days¹², tracheostomy^{12,16}, endotracheal intubation¹², body temperature^{15,18}, mean arterial pressure, respiratory rate, heart rate, Glasgow coma score, Glasgow coma score, serum sodium, hematocrit, alveolar-arterial gradient (A-a gradient), partial oxygen pressure, bicarbonate, serum potassium, creatinine.

STATISTICAL ANALYSIS

We present patient's baseline characteristics as number, percentage and median with interquartile

Table 1. Characteristics of the Patients			
Characteristic	APACHE Score<20	APACHE Score>20	P Value
Age (yr)			<0.001
Median	55.5	62.3	
Interquartile range	41.19-66.6	50.1-71.5	
Male sex-no. (%)	207 (63.1)	440 (61.1)	0.537
Cigarette smoking	105 (32.0)	219 (30.4)	0.604
Underlying medical condition-no. (%)			
Congestive heart failure	33 (10.1)	87 (12.1)	0.340
Diabetes mellitus	54 (16.5)	186 (25.8)	0.001
COPD	25 (7.6)	49 (6.8)	0.632
Chronic liver disease	9 (2.7)	42 (5.8)	0.031
Other medical history-no. (%)			
Prior third generation cephalosporin usage	59 (18.0)	176 (24.4)	0.020
Head trauma	26 (7.9)	18 (2.5)	<0.001
Tuberculosis	44 (13.4)	108 (15.0)	0.499
Post operation	62 (18.9)	133 (18.5)	0.868
Severe organ insufficiency or immunocompromised	12 (3.7)	127 (17.6)	<0.001
Severe organ insufficiency or immunocompromised and surgery	10 (3.0)	32 (4.4)	0.285
Hospitalization>5days	263 (80.2)	491 (68.2)	<0.001
Tracheostomy	32 (9.8)	40 (5.6)	0.013
Endotracheal intubation	296 (90.2)	668 (92.8)	0.161
Physical exam			
Body temperature (°C)			0.348
Median	37.2	37.3	
Interquartile range	36.8-38.0	36.7-38.3	
Mean arterial pressure (mmHg)			0.014
Median	86.3	83.3	
Interquartile range	78.3-97.7	71.3-98.7	
Respiratory rate (/min)			<0.001
Median	20.0	22.0	
Interquartile range	20.0-24.0	20.0-28.0	

Table 1. (Continued)

Characteristic	APACHE Score<20	APACHE Score>20	P Value
Heart rate (/min)			<0.001
Median	100.0	112.0	
Interquartile range	88.0-118.0	94.0-130.0	
Glasgow coma score			<0.001
Median	11.0	10.0	
Interquartile range	11.0-11.0	8.0-11.0	
Laboratory			
White blood cell (X103/ μ L)			0.029
Median	11.3	12.5	
Interquartile range	7.9-16.6	7.9-19.4	
Hematocrit(%)			<0.001
Median	33.1	29.4	
Interquartile range	28.0-37.8	24.8-35.0	
A-a gradient (If FiO ₂ <50%)			0.095
Median	52.0	48.0	
Interquartile range	30.0-92.0	24.0-78.0	
Partial oxygen pressure (If FiO ₂ >50%)			0.335
Median	179.0	163.0	
Interquartile range	125.0-251.0	117.1-234.9	
Bicarbonate (If no arterial blood gas)			<0.001
Median	24.4	21.0	
Interquartile range	22.0-26.6	17.8-24.9	
Serum sodium (mEq/L)			0.001
Median	137.0	136.0	
Interquartile range	134.0-140.0	131.0-141.0	
Serum potassium (mg/dl)			0.927
Median	3.8	3.8	
Interquartile range	3.4-4.2	3.2-4.5	
Creatinine (mg/dl)			<0.001
Median	1.0	1.6	
Interquartile range	0.7-1.3	0.9-2.9	

Table 2. Outcome of the Treatment

Outcome	APACHE Score<20	APACHE Score>20	Relative risk (95% CI)
Ventilator associated pneumonia-no. (%)	109 (33.2)	200 (27.8)	1.196 (0.986-1.452)
Death-no. (%)	119 (36.3)	280 (38.9)	0.933 (0.787-1.106)

ranges as appropriate. The chi-squared test was used to analyze categorical variables, such as sex and comorbidities, continuous variables were compared using the Mann-Whitney U test. To evaluate whether patients with a high APACHE II score were at higher risk of VAP than low APACHE II score, we calculated the relative risk (RR) with 95% confidence interval (CI) of VAP between patients with APACHE II score lower than 20 versus higher than 20.11 Then we used binary logistic regression adjusted for the following potential confounders of factors predicting VAP. Receiver operating characteristics (ROC) curves calculations were performed to compare sensitivity and specificity of the five factors that found to be associated with VAP and use cut-off values for predicting VAP in ICU. Statistical analyses were done with statistic software package.

RESULTS

PATIENTS' CHARACTERISTICS

Initially, they were 1,080 patients preliminary included into the present study. However, only 1,048 left for the analysis, 404 in the group of APACHE II score<20 and 644 in the group of APACHE II score>20. Majority of them were male (61.7%) with the median age of 60.5 years old. In those with APACHE II score<20, they tended to be younger ($P<0.001$), higher proportion of those

with head trauma ($P<0.001$), hospitalization more than 5 days (<0.001), tracheostomy ($P=0.013$), higher mean arterial pressure ($P=0.014$), higher Glasgow coma score ($P<0.001$), higher hematocrit ($P<0.001$), higher bicarbonate ($P<0.001$), higher blood sodium ($P=0.001$), higher A-a gradient ($P<0.001$) and lower proportion of those with Diabetes mellitus ($P=0.001$), chronic liver disease ($P=0.031$), prior third-generation cephalosporin usage ($P=0.020$), history of severe organ insufficiency or immunocompromised ($P<0.001$), lower respiratory rate (<0.001), lower heart rate (<0.001), lower white blood cell ($P=0.029$), lower creatinine (<0.001). However, the proportion of male sex, smokers, congestive heart failure, diabetes mellitus, COPD, tuberculosis, postoperative, history of severe organ insufficiency or immunocompromised and surgery, endotracheal intubation as well as their body temperature, serum potassium, and partial oxygen pressure were similar across the two groups.

OUTCOMES

From Table 2, we found that the occurrence of VAP and death^{19,20} were similar across the two groups (RR, 1.196; 95% CI 0.986 to 1.452; RR, 0.933; 95% CI 0.787 to 1.106, respectively). From Table 3, we found that cefoperazone plus sulbactam was the only significant factor associated with higher death rate ($P=0.032$).

Table 3. Infection and antibiotics use						
Infection and antibiotics	APACHE <20			APACHE>20		
	Survival	Death	P Value	Survival	Death	P Value
Gram-positive cocci-no. (%)						
<i>Methicillin-sensitive Staphylococcus aureus</i>	29 (13.9)	19 (16.0)	0.606	45 (10.2)	20 (7.1)	0.159
<i>Methicillin-resistant Staphylococcus aureus</i>	7 (3.3)	5 (4.2)	0.763	10 (2.3)	8 (2.9)	0.624
<i>Streptococcus pneumoniae</i>	2 (1.0)	2 (1.7)	0.623	6 (1.4)	3 (1.1)	1.000
Aerobic Gram-negative bacilli-no. (%)						
<i>Haemophilus influenzae</i>	3 (1.4)	2 (1.7)	1.000	1 (0.2)	1 (0.4)	1.000
<i>Lactose fermenting gram-negative bacilli</i>	14 (6.7)	3 (2.5)	0.101	18 (4.1)	14 (5.0)	0.564
<i>Pseudomonas aeruginosa</i>	31 (14.8)	24 (20.2)	0.214	53 (12.0)	33 (11.8)	0.917
<i>Acinetobacter baumannii</i>	48 (23.0)	39 (32.8)	0.053	93 (21.1)	65 (23.2)	0.511
<i>Klebsiella pneumonia</i>	34 (16.3)	25 (21.0)	0.282	66 (15.0)	46 (16.4)	0.606
Enterobacter spp.	28 (13.4)	21 (17.6)	0.299	55 (12.5)	35 (12.5)	1.000
<i>Burkholderia pseudomallei</i>	4 (1.9)	0	0.301	14 (3.2)	6 (2.1)	0.408
Antibiotics-no. (%)						
Aminoglycosides	3 (1.4)	3 (2.5)	0.672	8 (1.8)	4 (1.4)	0.774
Carbapenems	75 (35.9)	41 (34.5)	0.794	157 (35.7)	95 (33.9)	0.631
Cephalosporins						
First generation	17 (8.1)	14 (11.8)	0.280	15 (3.4)	13 (4.6)	0.404
Third generation	148 (70.8)	86 (72.3)	0.779	290 (65.9)	199 (71.1)	0.148
Vancomycin	27 (12.9)	19 (16.0)	0.445	68 (15.5)	45 (16.1)	0.824
Clindamycin	25 (12.0)	19 (16.0)	0.306	53 (12.0)	41 (14.6)	0.313
Macrolides	34 (16.3)	16 (13.4)	0.494	53 (12.0)	40 (14.3)	0.382
Penicillins	15 (7.2)	12 (10.1)	0.357	42 (9.5)	24 (8.6)	0.659
Penicillin combinations	62 (29.7)	37 (31.1)	0.787	136 (30.9)	85 (30.4)	0.876
Colistin	29 (13.9)	18 (15.1)	0.756	55 (12.5)	36 (12.9)	0.888
Fluoroquinolone	65 (31.1)	45 (37.8)	0.216	105 (23.9)	65 (23.2)	0.841
Sulfonamides	15 (7.2)	10 (8.4)	0.687	25 (5.7)	13 (4.6)	0.543
Fosfomycin	4 (1.9)	0	0.301	5 (1.1)	7 (2.5)	0.231
Metronidazole	41 (19.6)	16 (13.4)	0.156	76 (17.3)	43 (15.4)	0.500
Cefoperazone and sulbactam	49 (23.4)	41 (34.5)	0.032	112 (25.5)	77 (27.5)	0.543

Table 4. Factors Predicting Ventilator Associated Pneumonia

Factor	Adjusted odds ratio and 95% CI
Age	1.008 (0.998-1.017)
Male	0.878 (0.654-1.179)
APACHE II score	0.975 (0.941-1.009)
Cirrhosis	1.022 (0.507-2.057)
Congestive heart failure	1.410 (0.912-2.180)
Head trauma	1.799 (0.941-3.437)
Hospitalization>5 days	3.382 (2.297-4.980)
Tracheostomy	1.860 (1.019-3.397)
Endotracheal intubation	2.419 (1.236-4.731)
Diastolic blood pressure	1.011 (1.003-1.020)
Glasgow coma score	1.017 (0.951-1.087)
Diabetes mellitus	0.839 (0.592-1.191)
Hematocrit	0.991 (0.971-1.012)
Prior third generation cephalosporin usage	0.588 (0.403-0.857)
Post operation	1.495 (1.055-2.118)
Creatinine	1.033 (0.986-1.082)
White blood cell	1.013 (1.000-1.026)

FACTORS PREDICTING VAP

From Table 4, five factors were found to be associated with VAP. This included (i) history of prior prescribed with cephalosporin (AOR, 0.588; 95% CI 0.403 to 0.857), (ii) tracheostomy (AOR, 1.860; 95% CI 1.019 to 3.397), (iii) endotracheal intubation (AOR, 2.419; 95% CI 1.236 to 4.731), (iv) post-operation (AOR, 1.495; 95% CI 1.055 to 2.118), (v) hospital longer than 5 days (AOR, 3.382; 95% CI 2.297 to 4.980).

Receiver-operating-characteristic (ROC) curve shows the diagnostic performance of the model. It has an area under the curve (AUC) of 0.667 and at the optimal cut off point of score more

than 2.0, it yields a sensitivity of 79.6% and specificity of 49.0%.

DISCUSSION**MAIN FINDINGS**

In this retrospective cohort, we found that the incidence of ventilator-associated pneumonia in patients with APACHE II score more than 20 was not significantly different from that of those lower than 20. The incidence of ventilator-associated pneumonia decreased with the history of prior prescribed with cephalosporin while it increased with tracheostomy, endotracheal intubation, post-

Table 5. Accuracy of the factors predicting ventilator associated pneumonia

Factor	Area under the curve	P Value
Prior third generation cephalosporin usage	0.447	0.006
Tracheostomy	0.525	0.207
Endotracheal tube	0.518	0.362
Postoperation	0.552	0.008
Hospital longer than 5 days	0.612	<0.001
Predicting model*	0.665	<0.001

* The model was derived from the binary logistic regression with the given assigned score as (-0.5xprior third generation cephalosporin usage)+(2xtracheostomy)+ (1xendotracheal tube)+ (0.5xpost operation)+(1.5xhospital longer than 5 days).

operation and hospitalization longer than 5 days. We also found that the APACHE II score was not significantly associated with death. Cefoperazone plus sulbactam was the only significant factor associated with the higher death rate. Additionally, we made up the diagnostic test to predict VAP from five-factor that significantly associated with it. with a sensitivity of 79.6% and specificity of 49.0%.

COMPARISION WITH OTHER STUDIES

The purpose of the study was to examine whether the APACHE II score increases risk of VAP in ICU patients. It was the first study specifically looking at the association between APACHE II score and the VAP. In our study, we found that the occurrence of VAP and death were similar across the two groups of APACHE II score 20 or higher and those of lower

Table 6. Validity of the score from the predicting model

Score of the predicting model	Sensitivity	Specificity
-0.5	100	0.50
0	100	2.7
0.5	98.7	11.4
1	90.3	34.0
1.5	87.4	37.9
2	79.6	49.0
2.5	24.6	85.8
3	10.4	95.4
3.5	5.8	97
4	4.9	98

* The model was derived from the binary logistic regression with the given assigned score as (-0.5xprior third generation cephalosporin usage) +(2xtracheostomy)+ (1xendotracheal tube)+ (0.5xpost operation)+(1.5xhospital longer than 5 days).

than 20. This was contradicted by a Japanese study by Suka which examined the association between nosocomial infection in the ICU and the APACHE II score in more than 8,500 ICU patients.⁶ The result of Suka's study showed that high APACHE II score increased the risk of nosocomial infection.⁶ This might be due to our study has the fewer sample size to detect the association between APACHE II score and VAP. Moreover, we found that prior third-generation cephalosporin usage was significantly decreased the risk of VAP. This was also contradict to the results of Rello J's study which showed prior antibiotic therapy was the most important factors related to the causative flora of respiratory infections in mechanically ventilated patients²⁸ and the result of Eylem Sercan Özgür's study that which stated that prior use of antibiotics was the recognized factors increasing the risk of VAP.²⁶ These different findings might be due to the two previous studies were conducted in places with frequently unnecessary use of broad-spectrum antibiotics that would result in a selection favoring resistant bacteria and might not respond to the antibiotic use in the present study.

In our study, tracheostomy increased the risk of VAP. The findings were similar to those with the result of Ibrahim et al's study that also showed tracheostomy was independently associated with the development of VAP.¹⁰ The result of Kollef's study showed that patients receiving a tracheostomy were statistically more likely to develop VAP compared with patients without tracheostomy.²³ In our study, we found that endotracheal intubation was significantly associated with VAP. The following two studies also

showed that endotracheal intubation was associated with VAP; a study by Girou et al, in matched case-control study of 100 patients, found that rates of nosocomial pneumonia and all nosocomial infections were much lower in patients supported with noninvasive ventilation than those intubated and ventilated mechanically²⁴ and a study by Mann H. Kollef et al, in prospective cohort study of 521 patients, reported that reintubation or intubation was significantly associated with VAP.³⁵ Moreover, the present study, we found that patients admitted to the ICU after the operation that was significantly associated with VAP. This supported the previous study observed that urgent operation with high APACHE II score was significantly associated with VAP.⁶ We also found that hospitalization longer than 5 days was significantly associated with VAP similar to the findings from Oliveira, J's study which stated that hospitalization ≥ 5 days was risk factors of VAP.

LIMITATION OF THE STUDY

This study has several limitations. Firstly, this is a retrospective cohort using secondary data that might risk to bias and missing data. However, we tried to verify all the data before we collected on the data collection sheets as well as we excluded those with incomplete data. Secondly, the sample size of this study seemed to be fewer to detect the difference. Given the type 1 error of 5% and power of 80%. We required 2,707 patients (1,854 in the group of APACHE II score more than 20, and 853 in those lower than 20). Unfortunately, we had only 1,048 patients included in the present study. In the present study, we also found that cefoperazone

plus sulbactam was the only significant factor associated with higher death rate due to we use this drug in the severe patient.

CONCLUSION AND IMPLICATION

This study showed no evidence that APACHE II score more than 20 was associated with an increased risk of VAP. To determine the association more precisely between APACHE II score and VAP, the further study

needs larger sample size with a prospective design to collect the primary data for more accurate data. We suggest for close monitoring the patients that have a tracheostomy, endotracheal intubation, post-operation and hospitalization longer than 5 days for possible risk of VAP. The newly created model for predicting the incidence of VAP in the ICU patients is also useful for screening as it has high sensitivity.

ACKNOWLEDGMENTS & DECLARATION

The authors would like to thank .Thammasorn Jeeraumponwat, 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

REFERENCES

- 1.A Randomized Trial of Diagnostic Techniques for Ventilator-Associated Pneumonia – NEJM [Internet]. [cited 2014 May 7]. Available from: <http://www.nejm.org/doi/full/10.1056/NEJMoa052904#ref1>
- 2.Warren DKS SJ, Olsen MA, Kollef MH, Hollenbeak CS, Cox MJ, Cohen MM, Fraser VJ. Outcome and Attributable Cost of Ventilator-Associated Pneumonia among Intensive Care Unit Patients in a Suburban Medical Center*. CriticalCare Medicine 2003; 31:1312-1317.
- 3.Rello J, Paiva JA, Baraibar J, et al. International Conference for the Development of Consensus on the Diagnosis and Treatment of Ventilator-Associated Pneumonia. Chest 2001; 120:955-970.
- 4.Saad Ahmed Naved, Shahla Siddiqui and Fazal Hameed Khan. APACHE-II Score CorrelationWith Mortality And Length Of Stay In An Intensive Care Unit.
- 5.JSTOR: Infection Control and Hospital Epidemiology, Vol. 18, No. 12 (Dec., 1997), pp.825-830[Internet],[cited 2014 May 31]. Available from: <http://www.jstor.org/discover/10.2307/30141341?uid=27612&uid=3739136&uid=2&uid=3&uid=27609&uid=67&uid=62&sid=21104092973627>
- 6.Suka M, Yoshida K, Takezawa J. Association between APACHE II score and nosocomial infections in intensive care unit patients: A multicenter cohort study. Environ Health Prev Med. 2004 Nov;9(6):262-5.
- 7.Incidence and risk factors of pneumonia a... [Intensive Care Med. 1993] - PubMed - NCBI[Internet][cited 2014 May 31].Available from: <http://www.ncbi.nlm.nih.gov/pubmed/8408934>
- 8.Analysis of risk factors for... [Eur J Clin Microbiol Infect Dis. 2000] - PubMed - NCBI [Internet]. [cited 2014 May 31].available from <http://www.ncbi.nlm.nih.gov/pubmed/10947222>
- 9.Usefulness of severity indices in intensi... [Intensive Care Med. 1991] - PubMed - NCBI [Internet].[cited 2014 Jun 1].Available from: <http://www.ncbi.nlm.nih.gov/pubmed/1744324>
- 10.CHESTJournal|Article[Internet].[cited 2014 Jun 7].Available from: <http://journal.publications.chestnet.org/article.aspx?articleid=1079869>
- 11.Patient transport from intensive care increases the risk of developing ventilator-

- associated pneumonia [Chest. 1997] - PubMed - NCBI [Internet]. [cited 2014 May 31]. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/9315813>
12. Prevention of ventilator-associated pneumonia [Internet]. [cited 2014 May 7]. Available from: <http://www.elsevier.pt/en/revistas/revista-portuguesa-pneumologia-320/artigo/prevention-of-ventilator-associated-pneumonia-90304253>
13. Risk factors for hospital-acquired pneumonia outside the intensive care unit: A case-control study [Internet]. [cited 2014 May 7]. Available from: <http://www.sciencedirect.com/science/article/pii/S0196655313011012>
14. Risk factors for hospital-acquired pneumonia caused by carbapenem-resistant Gram-negative bacteria in critically ill patients: a multicenter study in Korea [Internet]. [cited 2014 May 7]. Available from: <http://www.sciencedirect.com/science/article/pii/S0732889313004574#>
15. Incidence, risk, and prognosis factors of ... [Am Rev Respir Dis. 1990] - PubMed - NCBI [Internet]. [cited 2014 May 31]. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/2202245>
16. Pneumonia due to Haemophilus influenzae among mechanic... [Chest. 1992] PubMed - NCBI [Internet]. [cited 2014 May 31]. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/1424890>
17. Risk Factors for Ventilator-Associated Pneumonia: From Epidemiology to Patient Management [Internet]. [cited 2014 May 7]. Available from: <http://cid.oxfordjournals.org/content/38/8/1141.long>
18. Factors predicting ventilator-associated pneumonia [Crit Care Med. 2003] - PubMed - NCBI [Internet]. [cited 2014 May 30]. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/12682479>
19. Risk factors for pneumonia and fatality in... [Am Rev Respir Dis. 1986] - PubMed - NCBI [Internet]. [cited 2014 May 31]. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/3706887>
20. Effect of ventilator-associated pn... [Am J Respir Crit Care Med. 1996] - PubMed - NCBI [Internet]. [cited 2014 May 31]. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/8680705>
21. American Thoracic Society Infectious Diseases Society of America. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. Am J Respir Crit Care. 2005;171:388-416.
22. Combes A, Figliolini C, Trouillet JL, Kassis N, Wolff M, Gibert C, et al. Incidence and outcome of polymicrobial ventilator-associated pneumonia. Chest. 2002;121:1618-23.
23. The Pathogenesis of Ventilator-Associated Pneumonia: Its Relevance to Developing Effective Strategies for Prevention [Internet]. [cited 2014 Jun 7]. Available from: <http://rcrcjournal.com/content/50/6/725.full.pdf+html>
24. Mann, H., Kollef. Patient Transport From Intensive Care Increases the Risk of Developing Ventilator-Associated Pneumonia. 3 SEPTEMBER 1997
25. Laupland KB, Kirkpatrick AW, Church DL, Ross T, Gregson DB. Intensive care Unit acquired bloodstream infections in a regional critically ill population.
26. Ventilator-associated pneumonia due to extensive drug-resistant Acinetobacter baumannii: Risk factors, clinical features, and outcomes [Internet]. [cited 2014 May 31]. Available from: <http://www.sciencedirect.com/science/article/pii/S0196655313012145>
27. Risk factors for infection by Acinetobacter baumannii ... [Chest. 1997] - PubMed - NCBI [Internet]. [cited 2014 May 31]. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/9377916>
28. Microbial causes of ventilator-associated... [Semin Respir Infect. 1996] - PubMed - NCBI [Internet]. [cited 2014 May 31]. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/8885060>

ORIGINAL ARTICLE BY

Pattarasinee Wongsanao¹, M.D.; Jutarat Anutragulchai², M.D.;
Krisana Nuangkhanthtree³, M.D., Tanatta Chinkijchan⁴, M.D.

¹Khamcha-I Hospital, Thailand, ²Si Chomphu Hospital, Thailand, ³Nong Hi Hospital, Thailand, ⁴Selaphum Hospital, Thailand

Accepted: April 2017
Latest revision: May 2017
Printed: August 2017

Correspondence to: Krisana Nuangkhanthtree;
k.nuangkhanthtree@gmail.com

ABSTRACT

OBJECTIVE

To identify the association between teenage pregnancy and birth asphyxia.

METHODS

We conducted a retrospective cohort with a nested case-control study by reviewing medical records of term primigravida pregnant women with adequate antenatal care (ANC) that delivered vaginally at Khon Kaen Hospital during January 2011-September 2013. In the analysis, we compared the rate of birth asphyxia between teenage pregnancy and that of adult pregnancy.

RESULTS

In the present study, there were 2,500 pregnant women eligible to be included initially, however, 1,472 pregnant women were excluded and left 1,028 for the analysis. The rate of birth asphyxia occurred in 2.4% of the teenage pregnancy group (13 from 541) as compared with 2.3% of the adult pregnancy group (11 from 487) (adjusted odds ratio [AOR], 1.07; 95% confidence interval [CI], 1.41 to 3.25; $P=0.88$). Findings in our nested case-control study using logistic regression revealed that the second stage of labor was the only significant risk factor for birth asphyxia (AOR, 1.020; 95% CI, 1.003 to 1.037). However, gestational age, peripartum fever, body mass index before pregnancy, contraceptive use, age, and body mass index before delivery were not associated with the occurrence of birth asphyxia.

CONCLUSION

Our results showed that the teenage pregnancy did not increase the rate of birth asphyxia and the duration of the second stage of labor increased rate of birth asphyxia.

INTRODUCTION

Birth asphyxia is a condition of impaired gas exchange occurring during labor leading to progressive hypoxia, as a consequence it is a major cause of neonatal mortality and neurological impairment.¹ Findings from previous studies have suggested the association between teenage pregnancy and birth asphyxia as teenage pregnancy or adolescent pregnancy is one of the major obstetric problems as it is a cause of many complications for both mother and child during antepartum, intrapartum and postpartum.^{2,3,4,5} However, evidence regarding the association between teenage pregnancy and birth asphyxia are relatively scant. Accordingly, this study aimed to ascertain the association of between teenage pregnancy and birth asphyxia.^{3,4}

In our study, conducted from January 2011 to September 2013, was a retrospective cohort with a nested case-control study designed to provide current and reliable data on the prevalences of the rate of birth asphyxia in teenage pregnancy compared with a rate of birth asphyxia in adult pregnancy.

METHODS

STUDY DESIGN

This was a non-concurrent cohort study reviewing the medical record from the hospital database which containing details of patients' data, medical diagnoses, and labor record sheet to test our pre-specified hypothesis that teenage pregnancy was associated with an increased rate of birth asphyxia.

PATIENTS

We performed a retrospective cohort with a nested case-control study involving pregnant women who had the vaginal delivery at Khon Kaen Hospital, that has study population of total 2500 people. All pregnant were 13 to 35 years old, were primigravidarum, with lived birth child, were term pregnancy and with antenatal care (ANC) more than 4 times were included in the analysis.

DATABASE AND OUTCOME

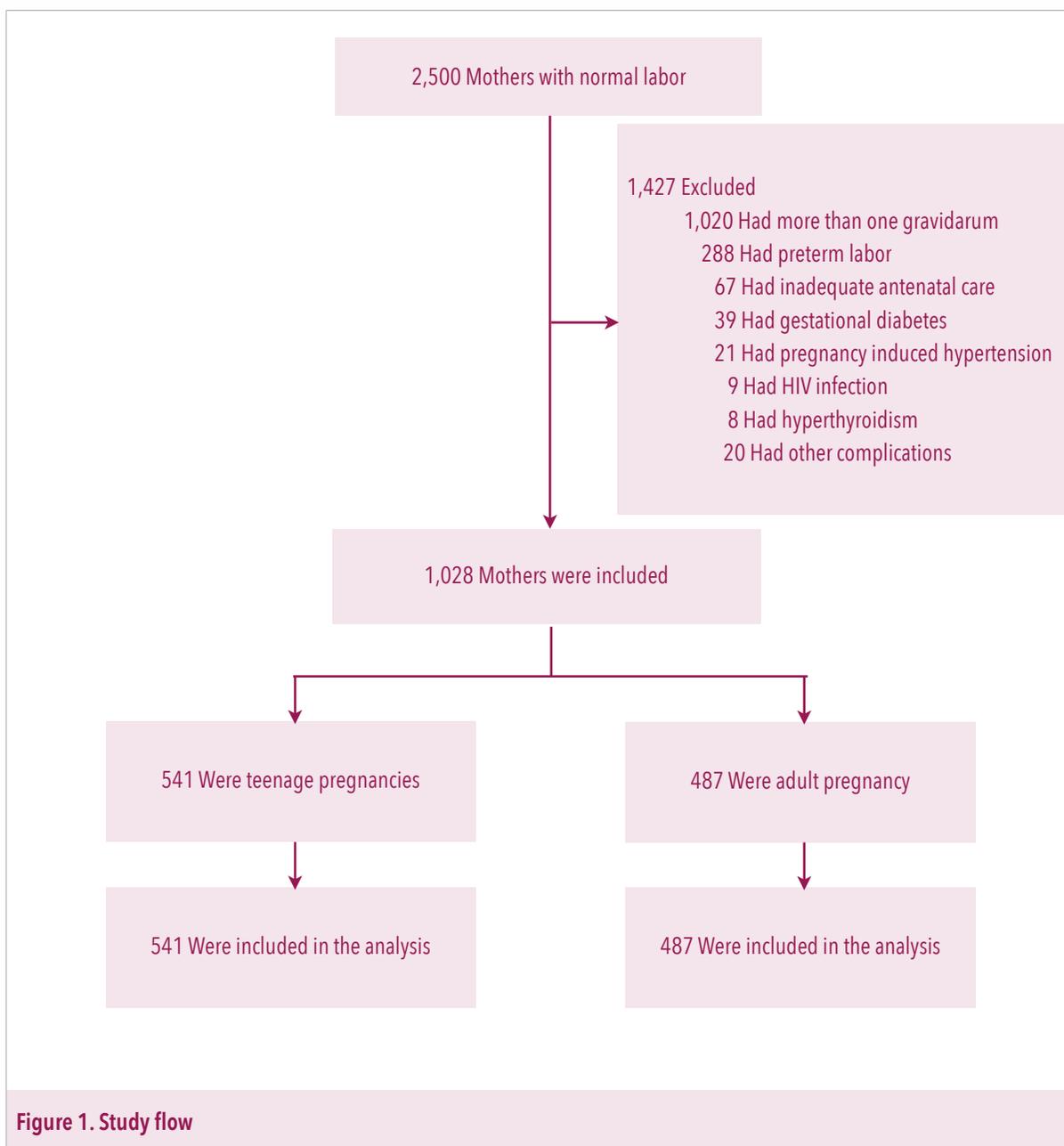
The clinical and demographic data related to pregnant women mentioned above were aggregated in Khon Kaen Hospital Database which included data regarding patient characteristics as well as clinical data prior to, during and postpartum periods.

Included variables were maternal age, gravidarum parity, gestational age at delivery (the number of days since the last men-strual period), mean arterial pressure(MAP), prepregnancy weight, weight before delivery, maternal height, pre-pregnant BMI, BMI before delivery, ANC, contraceptive use, self-reported smoking and alcohol drinking status as well as peripartum fever.

The outcomes included birth asphyxia as the primary outcome, Apgar score, birth weight, umbilical cord length, head circumference, meconium stain, body temperature, duration of stage labor. The potential confounders including parity, smoking and alcohol drinking status of the mothers, diabetes mellitus and peripartum fever (defined as a temperature of 38°C or higher of the mothers) were included in the multivariable; binary logistic regression analysis.⁴

Table 1.Characteristics of women who had a first pregnancy

Characteristic	Teenage pregnancy N=541	Adult pregnancy N=487	P Value
Age -- (yr)			<0.001
Median	18	24	
Interquartile range	17-19	22-26	
Gestational age--(week)			0.933
Median	39	39	
Interquartile range	38-40	38-40	
Number of ANC--(time)			< 0.001
Median	8	9	
Interquartile range	7-10	8-11	
Contraceptive use -- no. (%)	159 (30.3)	210 (44.3)	<0.001
Smoking -- no. (%)	4 (0.7)	3 (0.6)	0.807
Alcohol drinking -- no. (%)	12 (2.2)	10 (2.1)	0.843
Peripartum fever- no. (%)	37 (6.8)	27(5.5)	0.391
Pre-pregnancy weight--(kg)			0.87
Median	49	48.4	
Interquartile range	44-55	45-54	
Weight before delivery--(kg)			0.022
Median	62.6	63	
Interquartile range	56.9-69.0	58.8-70.1	
Height --(cm)			0.293
Median	158	158	
Interquartile range	155-162	155-162	
Pre-pregnancy BMI--(kg/m2)			0.826
Median	19.38	19.47	
Interquartile range	18.0-21.6	17.9-21.4	
BMI before delivery--(kg/m2)			0.007
Median	24.76	25.35	
Interquartile range	22.9-27.6	23.5-27.7	
Mean arterial pressure--(mmHg)			0.76
Median	88	87.33	
Interquartile range	81.4-93.3	82.7-93.3	



STATISTICAL ANALYSIS

Mean and standard deviation (SD) were used to describe normally distributed data, median and interquartile range for non-normally distributed data and number with percentage for categorical

data. Chi-square test was used to compare categorical variables between the two group regarding teenage and non-teenage pregnancy while Mann-Whitney U test for continuous variables. Binary logistic-regression models were

constructed to identify independent risk factors associated with neonatal birth asphyxia presenting in term of adjusted odds ratio (AOR) and its 95% confidence interval (CI).

RESULTS

PATIENTS' CHARACTERISTICS

There were 2,500 pregnant women delivered at Khon Kaen Hospital during the study period; 1,472 pregnant women were excluded and left 1,028 for the analysis (Figure 1). Detail of exclusion is presented in Figure 1. Their median age was 20 years old and their median gestational age was 39 weeks. The median of the number of ANC was 9 times, contraceptive was used in 369 mothers, seven mothers were smokers and 22 mothers were alcohol drinker. Sixty-four mothers had a peripartum fever. The median of pre-pregnancy weight was 49 kilograms and their median of weight before delivery was 63 kilograms. The median height was 158 cm, their pre-pregnancy BMI was 19.5 kg/m² and their median BMI before delivery was 25.0 kg/m². Their median MAP was 88 mmHg. Characteristics of the mothers who were teenage pregnancy and adult pregnancy are also summarized in Tables 1. Comparing the teenage pregnancy group with the adult pregnancy group, the former tended to have a fewer number of ANC ($P < 0.001$), less proportion of those with contraceptive use ($P < 0.001$), lighter weight before delivery ($P = 0.022$) and lower BMI before delivery ($P = 0.007$). However, the other characteristics between the two groups were relatively similar.

OUTCOMES

A total of 24 infants with birth asphyxia were identified; 1.3% (13 of 541 infants) of the teenage mother group and 1.1% (11 of 487 infants) of the adult mother group (OR=1.065, $P = 0.878$) (Table 2). Comparing secondary outcomes between teenage pregnancy group and the adult group, the former tended to have a shorter duration of the second stage of labor ($P < 0.001$). However, other secondary outcomes tended to be similar between the two groups.

FACTORS AFFECTING ADVERSE OUTCOMES

Findings in our nested case-control analysis using logistic regression, the risk factors found to be associated with birth asphyxia included the second stage of labor was increased (AOR, 1.0; 95% CI, 1.008 to 1.050; $P = 0.006$). However, age, gestational age, contraceptive use, BMI before delivery and peripartum fever were not associated with birth asphyxia (Table 3).

DISCUSSION

MAIN FINDINGS

We found no evidence of the association between teenage pregnancy and birth asphyxia as in the conventional analyses, teenage pregnancy did not increase risk of birth asphyxia compared with adult pregnancy. In our study, the teenage pregnancy group and the adult pregnancy group produced relatively similar outcomes. We also found that the prolonged the second stage of labor was the only factor that increased the rate of birth asphyxia.

Table 2. Primary and secondary outcomes

Outcome	Teenage pregnancy N = 541	Adult pregnancy N = 487	P Value
Birth asphyxia -- no. (%)	13 (2.4)	11 (2.3)	0.878
Infant male sex -- no. (%)	275 (50.8)	251 (51.5)	0.821
Apgar			
1 min			0.992
Median	10	10	
Interquartile range	9-10	9-10	
5 min			0.217
Median	10	10	
Interquartile range	10-10	10-10	
10 min			0.068
Median	10	10	
Interquartile range	10-10	10-10	
Birth weight -- (kg)	3005.8 _± 360.3	3045.8 _± 360.6	0.076
Umbilical cord length-- (cm)			0.387
Median	50	50	
Interquartile range	42.75-50	40-55	
Head circumference-- (cm)			0.185
Median	32	33	
Interquartile range	31.5-33	32-33	
Chest circumference -- (cm)			0.468
Median	32	32	
Interquartile range	31-33	31-33	
Meconium stain -- no. (%)			0.153
Clear	499 (85.9)	400 (86.6)	
Mild meconium	42 (8.0)	45 (9.7)	
Thick meconium	32 (6.1)	17 (3.7)	

Table 2. (Continued)

Outcome	Teenage pregnancy N = 541	Adult pregnancy N = 487	P Value
Body temperature -- (c)			0.155
Duration of labor			
First stage of labor			0.156
Median	555	585	
Interquartile range	370-780	410-800	
Second stage of labor			<0.001
Median	15	18	
Interquartile range	10-23	11-30	
Third stage of labor			0.234
Median	5	5	
Interquartile range	4-8	4-7	

Plus minus values are mean±SD

STRENGTH AND LIMITATION

The strengths of the current study were that detailed information of neonatal and pregnancy outcomes was very completed with availability more than 99% of the variables. Our conclusion was based on a large database of the tertiary care hospital. However, our study was still prone to recall bias as a nature of the retrospective study. For instance, self-reported smoking and alcohol drinking status were not validated by history taking and interview. Many evaluators (midwives nurse) might also affect the evaluation of maternal and fetal outcomes due to their subjectivity assessment. The further limitations of our study are that we cannot control the socioeconomic factors of each person and family that effects to the maternal self-care at home. Moreover, this study design was

prone to potential missing data of maternal history and status as well as those of the infants, without verification of data of medical records which might lead to under-reporting or over-reporting of the outcomes.

COMPARISON WITH OTHER STUDIES

In our study, Apgar at fifth minute was not associated with birth asphyxia. However, in the previous study, they found that Apgar at fifth minute was not associated with birth asphyxia but it can predict neonatal mortality rate. In previous data, they found more cases of birth asphyxia in short- and long-cord groups as compared to cords with normal length.²² However, we found no association between umbilical cord length and teenage pregnancy. From previous data, they found

Table 3. Binary logistic regression analysis for adverse perinatal outcome

Exposure	Adjusted odds ratio (95% CI)	P Value
Age	1.043 (0.927-1.173)	0.483
Gestational age	1.240 (0.812-1.894)	0.32
Duration of 2nd stage of labor	1.029 (1.008-1.050)	0.006
Contraceptive use	0.399 (0.139-1.145)	0.088
Peripartum fever	0.000 (0.000-0.000)	0.999

the association between head circumference and the rate of death from cardiovascular disease²³ but in our study, we found no association between head circumference and teenage pregnancy. In our study, we found no association between meconium stain and teenage pregnancy. In the previous study, they found that meconium aspiration syndrome developed in the meconium-stained neonates.²⁵ In our study, we found no association between neonatal body temperature and teenage pregnancy. In previous study, they found that neonates in hypothermia group were associated death or moderate or severe disability.

The previous research had studied about teenage pregnancy, they found many outcomes such as preterm delivery, low birth weight,

congenital malformations, stillbirth, Apgar score, and fetal pulmonary maturity.^{1 2 3 4 5 6} In previous study, they did not study about birth asphyxia in teenage pregnancy. Therefore, we designed the research to compare the rate of birth asphyxia between teenage pregnancy and adult pregnancy.

CONCLUSION AND IMPLICATION

Our results showed that the teenage pregnancy did not increase the rate of birth asphyxia and prolong the duration of the second stage of labor significantly increased the risk of birth asphyxia. Thus, we recommend to monitor the second stage of labor such as fetal heart sound, maternal blood pressure and keep its duration less than 2 hours to prevent birth asphyxia.

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

REFERENCES

1. Al-Macki N, Miller SP, Hall N, Shevell M. The spectrum of abnormal neurologic outcomes subsequent to term intrapartum asphyxia. *Pediatr Neurol*. December 2009;41(6):399-405.
2. Areemit R, Thinkhamrop J, Kosuwon P, Kiatchoosakun P, Sutra S, Thepsuthammarat K. Adolescent pregnancy: Thailand's national agenda. *J Med Assoc Thai Chotmaihet Thangphaet*. July 2012;95 Suppl 7:S134-142
3. Shuaib AA, Frass KA, Al-Harazi AH, Ghanem NS. Pregnancy outcomes of mothers aged 17 years or less. *Saudi Med J*. February 2011;32(2):166-70.
4. Matok I, Gorodischer R, Koren G, Sheiner E, Wiznitzer A, Levy A. The Safety of Metoclopramide Use in the First Trimester of Pregnancy. *N Engl J Med*. 2009;360(24):2528-35.
5. Sirakov M. [Congenital malformations in teenage pregnancy]. *Akusherstvo Ginekol*. 2012;51(4):35-40.
6. Iyoke CA, Ugwu GO, Ezugwu FO, Lawani OL, Onyebuchi AK. Retrospective cohort study of the effects of obesity in early pregnancy on maternal weight gain and obstetric outcomes in an obstetric population in Africa. *Int J Womens Heal*. August 14 2013;5:501-7.
7. Barrett JFR, Hannah ME, Hutton EK, Willan AR, Allen AC, Armson BA et. al. A Randomized Trial of Planned Cesarean or Vaginal Delivery for Twin Pregnancy. *N Engl J Med*. 2013;369(14):1295-305.
8. Landon MB, Spong CY, Thom E, Carpenter MW, Ramin SM, Casey B et. al. A Multicenter, Randomized Trial of Treatment for Mild Gestational Diabetes. *N Engl J Med*. October 1 2009;361(14):1339-48.
9. Malizia BA, Hacker MR, Penzias AS. Cumulative Live-Birth Rates after In Vitro Fertilization. *N Engl J Med*. 2009;360(3):236-43.
10. Winner B, Peipert JF, Zhao Q, Buckel C, Madden T, Allsworth JE et. al. Effectiveness of Long-Acting Reversible Contraception. *N Engl J Med*. 2012;366(21):1998-2007.
11. Tomedi LE, Simhan HN, Chang C-CH, McTigue KM, Bodnar LM. Gestational Weight Gain, Early Pregnancy Maternal Adiposity Distribution, and Maternal Hyperglycemia. *Matern Child Health J*. 1-6.
12. Radlowski EC, Johnson RW. Perinatal iron deficiency and neurocognitive development. *Front Hum Neurosci*. 2013;7:585.
13. Catalano PM, McIntyre HD, Cruickshank JK, McCance DR, Dyer AR, Metzger BE et. al. The Hyperglycemia and Adverse Pregnancy Outcome Study. *Diabetes Care*. April 2012;35(4):780-6.
14. Yu CKH, Khouri O, Onwudiwe N, Spiliopoulos Y, Nicolaides KH. Prediction of pre-eclampsia by uterine artery Doppler imaging: relationship to gestational age at delivery and small-for-gestational age. *Ultrasound Obstet Gynecol*. 2008;31(3):310-3.
15. Srisupundit K, Wanapirak C, Sirichotiyakul S, Tongprasert F, Leuwan S, Traisrisilp K. Hemoglobin levels and red blood cell indices in mid-gestational fetuses with beta-thalassemia/HbE, beta-thalassemia trait or Hb E trait and normal fetuses. *Prenat Diagn*. 2013;1-4.
16. Krueger PM, Scholl TO. Adequacy of prenatal care and pregnancy outcome. *JAOA J Am Osteopat Assoc*. January 8 2000;100(8):485-92.
17. Tezcan S, Adali T. Marriage characteristics and reproductive health of adolescents in Turkey: findings from Demographic and Health Surveys 1998 and 2008. *Turk J Pediatr*. June 2012;54(3):273-82.
18. Kingston D, Heaman M, Fell D, Chalmers B. Comparison of Adolescent, Young Adult, and Adult Women's Maternity Experiences and Practices. *Pediatrics*. January 5 2012;129(5):e1228-e1237.
19. Rubin SE, Davis K, McKee MD. New York City Physicians' Views of Providing Long-Acting Reversible Contraception to Adolescents. *Ann Fam Med*. March 2013;11(2):130-6.
20. Kahn JG, Brindis CD, Gleib DA. Pregnancies averted among U.S. teenagers by the use of contraceptives. *Fam Plann Perspect*. February 1999;31(1):29-34.
21. Casey BM, McIntire DD, Leveno KJ. The Continuing Value of the Apgar Score for the Assessment of Newborn Infants. *N Engl J Med*. 2001;344(7):467-71.
22. Balkawade NU, Shinde MA. Study of Length of Umbilical Cord and Fetal Outcome: A Study of 1,000 Deliveries. *J Obstet Gynecol India*. October, 1 2012;62(5):520-5.
23. Barker DJ, Osmond C, Simmonds SJ, Wield GA. The relation of small head circumference and thinness at birth to death from cardiovascular disease in adult life. *BMJ*. February, 13 1993;306(6875):422-6.
24. Mullany LC, Darmstadt GL, Khatry SK, LeClerq SC, Tielsch JM. Relationship between the surrogate anthropometric measures, foot length and chest circumference and birth weight among newborns of Sarlahi, Nepal. *Eur J Clin Nutr*. 2006;61(1):40-6.

25. Wiswell TE, Tuggle JM, Turner BS. Meconium Aspiration Syndrome: Have We Made a Difference? *Pediatrics*. January, 5 1990;85(5):715-21.

26. Bauer K, Pyper A, Sperling P, Uhrig C, Versmold H. Effects of Gestational and Postnatal Age on Body Temperature, Oxygen

Consumption, and Activity during Early Skin-to-Skin Contact between Preterm Infants of 25-30-Week Gestation and Their Mothers. *Pediatr Res*. 1998;44(2):247-51.

27. Menticoglou SM, Manning F, Harman C, Morrison I. Perinatal outcome in relation to

second-stage duration. *Am J Obstet Gynecol*. 1995;173(3, Part 1):906-12.

28. Matok I, Gorodischer R, Koren G, Sheiner E, Wiznitzer A, Levy A. The Safety of Metoclopramide Use in the First Trimester of Pregnancy. *N Engl J Med*. 2009;360(24):2528-35.





"I shall either find a way or make one"

-Hannibal Barca



THE
CLINICAL
ACADEMIA

@thaimaf

