Kuwait Board of Dermatology - Faculty of Dermatology

KUWAIT BOARD OF DERMATOLOGY

Kuwait Institute for Medical Specialization

KBD MEDICAL RESEARCH GUIDE

Prepared By:

Hasan Ashkanani M.D.
Danah Al-Kandari M.D.
Rawan Al-Mutairi M.D.
Ahmed Al-Sarraf M.D.

Hasan Ashkanani, Fatemah Al-Juaidi, Abeer Al-Bazali
First Edition, Reviewed February, 2024

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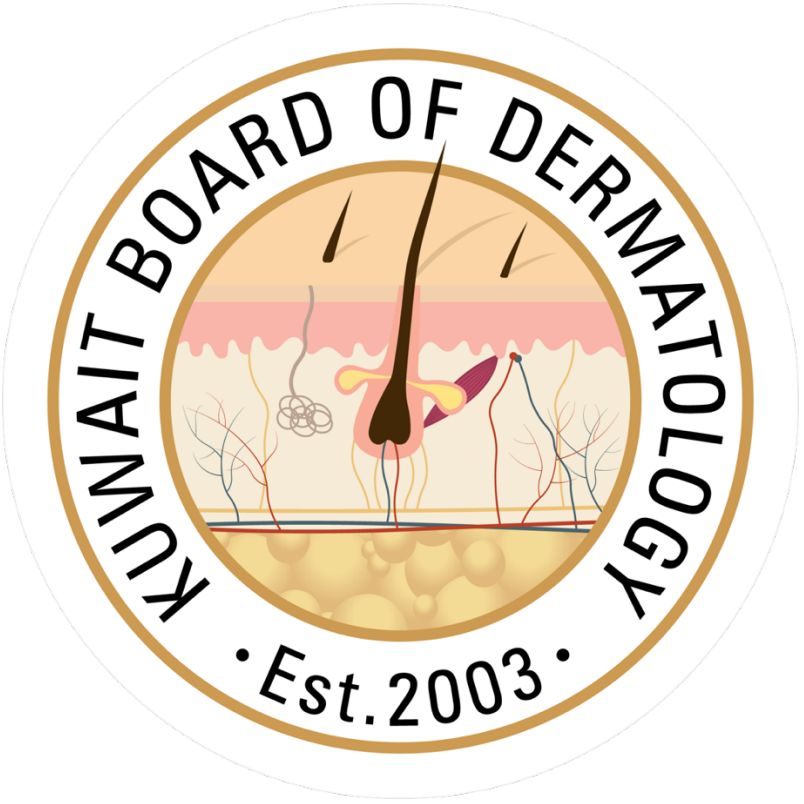

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Table of Contents

1. Credits:

- Authors:
    - Hasan Ashkanani M.D. (Credits, Introduction, Step I, Step V, Step IX, Appendix, Editing, Compilation).
    - Rawan Al-Mutairi M.D. (Step II, Step III, Step VI).
    - Ahmad Al-Sarraf M.D. (Step VII, Step VIII).
    - Danah Al-Kandari M.D. (Step IV, Step X, Step XI).
- Final approval was provided by Dr. Abeer Al-Bazali (Program Director) and Dr. Fatemah Al-Juaidi (Vice Program Director).
- Final Review was conducted by Dr. Arun Joshi (Head of Research Committee) and Hasan Ashkanani M.D.

2. Introduction

- Research plays a crucial role in comprehending issues affecting individuals, communities, and health systems. It facilitates a methodical and scientific evaluation of problems, often yielding knowledge that drives positive change, thereby enhancing the quality of healthcare. Without research, organizations and health institutions cannot advance or prosper.
- The Kuwait board of dermatology is a 5-year training program, during which residents are equipped with the medical knowledge and toolset needed for individual practice and participation in literary development of the field of Dermatology.
- As a residency program, the Kuwait Board of Dermatology implores its residents to be active beacons in the field of research, in order to further improve the science of dermatology, as well as improve healthcare services to patients with dermatological education.
- Starting in the academic year 2022-2023, the program started a major overhaul in the program curriculum, components, evaluation, and tasks assigned to the residents. This was done by adopting the Competence-By-Design (CBD) format used by the Royal College of Physicians and Surgeons in Canada.
- As a part of this transfer, a large emphasis on academic research was implemented in the residency program. This emphasis mandated that starting in the academic year that followed (2023-2024), residents must enroll in or start a research project in the field of dermatology.

- This idea was implemented as a means of involving residents in the field of research, creating further interest in the current state of dermatology in Kuwait, and encouraging resident-resident and resident-staff collaboration.
- Involvement in medical research, however, is not an easy task, and residents must have a supervision and mentorship in order to be able to excel in their projects.
- This document was made with the intention of creating a comprehensive medical research guide for residents enrolled in the Kuwait Board of Dermatology.
- The handbook adopts a step-by-step approach to crafting a research project, from conception of idea to the entire completion and publishing of the study.

3. Step I: Conception of Research Idea:

- Conception of the research topics is the first step of medical research. The conception takes the form of choosing the research topic.
- Choosing a research topic can be tricky, but tricks can simplify the selection process.
- It is recommended for the selection to be the result of answering questions. The following are some examples of questions that aid in the selection process:
    1. "What undiscovered thing do I want to unveil by doing this study?"
    2. "Do I have the access to recourses for sample selection?"
    3. "What do I want to add to the existing literature by conducting this study?"
- Conducting research can unveil a novel idea, or it can be inspired by different already existing papers in the literature, albeit still revealing something new that adds to the literature in your region.
- It is recommended to do some review in the existing literature for inspiration or to check if the idea is truly novel, as sometimes, some studies one can choose or think about are already conducted and well-established in the literature. Literature review guide is provided in step II of this manual.
- It is also recommended to take timeline, material availability, sample availability, and applicability in the region into account when selecting a study.
- Upon finalizing the study selection process, it is recommended to create a preliminary title for the study chosen, as it will be needed for the study proposal and ethical approval creation, explained in steps V, VI.

4. Step II: Literature Review

- This step includes two main instructions:
    1. How to perform literature review
    2. How to critically appraise a study

- **How to perform literature review**
- A literature review is a summary of the published work in a field of study.
- This can be a section of a larger paper or article, or can be the focus of an entire paper.
- Literature reviews show that you have examined the breadth of knowledge and can justify your thesis or research questions.
- They are also valuable tools for other researchers who need to find a summary of that field of knowledge.
- Here, we discuss the steps of writing a literature review.
    1. Determine your purpose and define your research scope
        - Work out what you need to address in the literature review.
        - What are you being asked to do in your literature review?
        - What are you searching the literature to discover?
        - Check your assignment question and your criteria sheet to know what to focus on.

2. Identify the literature
    - Select appropriate source material: Use a variety of academic or scholarly sources that are relevant, current and authoritative like pubmed and medline.
    - An extensive review of relevant material will include — books, journal articles, reports, government documents, conference proceedings and web resources.
    - Use Google Scholar or Scopus to find other sources that have cited a particular work
3. Analyse the literature you have found
    - In order for your writing to reflect strong critical analysis, you need to evaluate the sources.
    - For each source you are reviewing ask yourself these questions:
        - What are the key terms and concepts?
        - How relevant is this article to my specific topic?
        - What are the major relationships, trends and patterns?
        - How has the author structured the arguments?
        - How authoritative and credible is this source?
        - What are the differences and similarities between the sources?
        - Are there any gaps in the literature that require further study?
4. Write the review
    - Start by writing your thesis statement.
    - This is an important introductory sentence that will tell your reader what the topic is and the overall perspective or argument you will be presenting.

- Like essays, a literature review must have an introduction, a body and a conclusion.

- **<u>Structure of a literature review:</u>**

1. Introduction
    - Your introduction should give an outline of:
        - Why you are writing a review, and why the topic is important
        - The scope of the review — what aspects of the topic will be discussed
        - The criteria used for your literature selection (e.g. type of sources used, date range)
        - The organizational pattern of the review.
2. Body paragraphs
    - Each body paragraph should deal with a different theme that is relevant to your topic.
    - You will need to synthesize several of your reviewed readings into each paragraph, so that there is a clear connection between the various sources.
    - You will need to critically analyze each source for how they contribute to the themes you are researching.
    - The body could include paragraphs on:
        - Historical background
        - Methodologies
        - Previous studies on the topic
        - Mainstream versus alternative viewpoints

- Principal questions being asked
- General conclusions that are being drawn.

3. Conclusion
    - Your conclusion should give a summary of:
        - The main agreements and disagreements in the literature
        - Any gaps or areas for further research
        - Your overall perspective on the topic.

- **<u>Literature Review Checklist:</u>**
- Have I:
    1. outlined the purpose and scope?
    2. identified appropriate and credible (academic/scholarly) literature?
    3. recorded the bibliographical details of the sources?
    4. analyzed and critiqued your readings?
    5. identified gaps in the literature and research?
    6. explored methodologies / theories / hypotheses / models?
    7. discussed the varying viewpoints?
    8. written an introduction, body and conclusion?
    9. checked punctuation and spelling?

- When the answer is yes to all 9 questions, congratulations. You have just completed your literature review and can move on to Step III.

- **How to Critically Appraise a Study:**

- Critical appraisal is the process of carefully and systematically examining research to judge its trustworthiness, and its value and relevance in a particular context. Initial evaluation of an article published in literature should be based on certain core questions. These may include querying what could be the key learning points in the article, about its clinical relevance, if the study has a robust methodology, if the results are reproducible and could there be any bias or conflict of interest.
- Critical appraisal allows us to:
    1. Reduce information overload by eliminating irrelevant or weak studies
    2. Identify the most relevant papers
    3. Distinguish evidence from opinion, assumptions, misreporting, and belief
    4. Assess the validity of the study
    5. Assess the usefulness and clinical applicability of the study
    6. Recognize any potential for bias.
- How to critically appraise a paper: Some key questions to consider when critically appraising a paper:
    1. Is the study question relevant to my field?
    2. Does the study add anything new to the evidence in my field?
    3. What type of research question is being asked?
    4. A well-developed research question usually identifies three components
        - The group or population of patients
        - The studied parameter (e.g. a therapy or clinical intervention)
        - Outcomes of interest.
    5. Was the study design appropriate for the research question?

6. Did the methodology address important potential sources of bias?
    - Bias can be attributed to chance (e.g. random error) or to the study methods (systematic bias).
7. Was the study performed according to the original protocol?
    - Deviations from the planned protocol can affect the validity or relevance of a study.
8. Does the study test a stated hypothesis?
    - Is there a clear statement of what the investigators expect the study to find which can be tested, and confirmed or refuted.
9. Were the statistical analyses performed correctly?
    - The approach to dealing with missing data, and the statistical techniques that have been applied should be specified.
    - Original data should be presented clearly so that readers can check the statistical accuracy of the paper.
10. Do the data justify the conclusions?
    - Watch out for definite conclusions based on statistically insignificant results, generalized findings from a small sample size, and statistically significant associations being misinterpreted to imply a cause and effect.
11. Are there any conflicts of interest?
12. Who has funded the study and can we trust their objectivity? Do the authors have any potential conflicts of interest, and have these been declared?

5. Step III: Choosing a Study Design

- In medical research, we attempt to study the multitude of constantly changing and interrelated biologic processes that comprise human physiology. In order to make meaningful conclusions from the abundance of physiologic data available, we need to carefully consider the design of our investigations.
- We must meticulously define our study hypotheses, patient population, and research methods for our conclusions to be valid and our study a useful addition to the medical literature.
- "Study design" encompasses the deliberate planning of each level of the research process depicted in Figure-1.
- All levels of this process from initial planning to data analysis and interpretation are subject to the introduction of errors and statistical biases.

Initial planning
⇓
Research protocol design
⇓
Investigational review board (IRB) approval
⇓
Data collection
⇓
Data processing
⇓
Data analysis
⇓
Interpretation
⇓
Publication

Figure-1 (Research Process)

- We must anticipate and account for these potential sources of error at the outset if our study conclusions are to be valid.
- The goal in designing any research study, therefore, is to avoid systematic errors and biases as it is much easier to correct flaws in study design prior beginning a study rather than during or after concluding a study.
- Figure-2 illustrates the important elements to consider in the design of a research study.

- Type of study
- Method of treatment allocation
- Sample size necessary
- Creation of study protocol
- Choice of outcome measures
- Nature of data required
- Validation of data collected
- Choice of statistical analysis

Figure-2 (Elements of study design)

Types of Studies:

- Scientific studies can be divided into two basic types according to whether or not we administer an intervention or treatment.
  1. Observational studies:
     - involve the surveillance of one or more groups of patients to determine the effect of various patient characteristics on one or more outcome variables.
     - These patients, however, receive no intervention or treatment.
     - Observational studies demonstrate the “association", if any, between the patient characteristics and outcome variables of interest.
  2. Experimental studies:
     - involve the administration of an intervention or treatment to two or more groups of patients with attention being directed to identifying the impact the intervention has on a particular outcome.
     - Experimental studies, through demonstrating a response to therapy, may prove “causation”.
- We can also subdivide research studies by the time course of data collection (Figure-3).
  1. Longitudinal studies involve the analysis of data collected over an extended period of time and are thus able to identify the changing nature of a disease process.
  2. Prevalence studies, on the other hand, involve the analysis of data obtained at a single point in time and are useful in identifying the presence of disease in a particular patient population.
  3. Retrospective studies are longitudinal studies that look back in time to evaluate the factors affecting a particular variable of interest.

4. Prospective studies are longitudinal studies that look forward in time to analyze the impact of an intervention or disease process on the outcome variable(s) of interest.

- Retrospective studies are frequently easier to perform, but are more subject to potential errors and statistical biases. Prospective studies are usually more difficult to perform, more expensive, and more time consuming, especially if the disease of interest is rare. They provide more evidence for causality, however, than does a retrospective study.

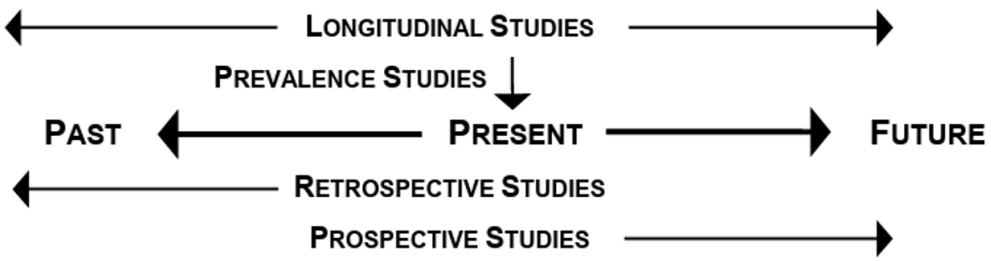


Figure-3 (Study design and the time course of data collection)

Observational Studies:

Case-series, case-control, cross-sectional, and cohort studies are all examples of observational studies.

1) **Case-series** studies are simply descriptive reports illustrating observations of interest on one or more, usually consecutive, patients. There are no control patients involved or initial hypotheses presented, although such studies frequently result in hypotheses that lead to further studies. Because they describe the disease course of the patients involved, they are longitudinal in design. An example of a case-series study is one that describes a hospital's last 50 patients with malignant thymoma, detailing their demographics, response to therapy, and survival.
2) **Case-control** studies are retrospective studies that identify a disease or outcome variable and look back in time to determine the risk factors that led to the disease. They compare a control population (patients without the disease) with a case population (patients with the disease) to identify factors that make the two groups different and may account for the occurrence of the disease. It is important to remember that observational studies, such as case-control studies, can only imply association and cannot prove causality. Case-control studies are also longitudinal studies as they review data from an extended period of time to arrive at their conclusions. An example of a case-control study is one that evaluates patients with and without colon cancer to determine whether differences in dietary or environmental factors may result in the development of malignancy.
3) **Retrospective studies**, such as the case-control design, are subject to a number of potential errors and statistical biases that are not present in prospective

studies. One of the more practical problems in performing a study using historical control patients is that we must assume that the data were collected accurately and recorded correctly in the patient's chart. This is not always the case and, unlike in a prospective study, we do not have access to the patients to remeasure the necessary information. Another common problem is that the necessary data may either not be present in the records or was unavailable at that time. For example, historical controls from the 1960's will not have computed tomography reports to compare with those of patients in the 1980's as this technology did not exist until 1974.

4) **Cross-sectional** studies are prevalence studies which collect data at a discrete point in time in order to answer particular questions about the status of the population at that instant. Disease prevalence studies, surveys, questionnaires, and meta-analyses are examples of cross-sectional studies. Cross-sectional studies are also frequently used to show "association" and suggest future studies.
5) **Cohort studies** are longitudinal studies which follow a group of patients with a common characteristic and collect data prospectively to answer questions related to the outcome variables of interest. This is the strongest of the observational study designs in that it is the least subject to statistical biases and errors in data recall and collection due to its prospective nature.

Experimental Studies:

- Experimental studies prospectively evaluate the efficacy of an intervention or treatment against another treatment.
- They can be either uncontrolled or controlled.
    1. Uncontrolled studies describe the effect of an intervention or treatment in a single group of patients. This type of study is uncontrolled because it makes no comparison with another treatment or no treatment at all. Thus, this design does not account for the effect of confounding variables on study outcome. It may, therefore, be difficult to interpret the results of such studies as we can never be sure that the treatment effect we see is due to the intervention and not due to the effect of a confounding variable. If the natural course of a disease process is predictable, a control group is less important.
    2. Controlled studies compare the impact of an intervention on two or more groups of patients. They compare the treatment group which receives the intervention to a control group which does not or which receives a different intervention that is frequently the current standard of treatment. Properly designed controlled studies equally distribute the potential sources of error discussed for uncontrolled studies between both the treatment and control groups. The effect of these errors will then tend to “cancel” each other out in the statistical analysis. Controlled studies are therefore statistically stronger than uncontrolled trials and are frequently necessary to adequately prove causality.

6. Step IV: Supervisor Allocation and Team Assembly

- Supervision Allocation:
    1. Identify Mentors: Look for faculty with expertise in your area of interest who have a track record of guiding residents.
    2. Set Expectations: Clearly communicate goals, timelines, and responsibilities with your supervisors.
    3. Regular Updates: Plan for consistent meetings or progress reports to maintain guidance and accountability.
- Team Assembly:
    1. Assess Skills: Identify the skills necessary for your research project (e.g., biostatistics, literature review, clinical expertise).
    2. Recruit Team Members: Involve residents and faculty who can contribute the needed skills and share a common interest in the research topic.
    3. Define Roles: Assign specific roles and responsibilities to each team member to prevent overlap and ensure comprehensive coverage of tasks.
- Deciding the Type of Study:
    1. Establish Goals: Determine the research question and what you aim to accomplish (e.g., proving a hypothesis, looking at prevalence).
    2. Consider Resources: Evaluate available resources including time, funds, and access to the patient population.

3. Choose Study Design: Select a design that aligns with your goals, such as cross-sectional, cohort study, case-control study, or randomized controlled trial (RCT).

- Timeline Considerations:
    1. Develop a Timeline: Estimate time for literature review, protocol development, IRB approval, data collection, analysis, and manuscript preparation.
    2. Set Milestones: Break the timeline into chunks with specific targets to enable measurable progress.
    3. Flexibility: Build extra time into the schedule for unexpected delays or additional data collection.
- Statistical Power and Sample Size:
    1. Consult a Biostatistician: Early involvement of a biostatistician can inform the study design and analysis.
    2. Power Analysis: Conduct power analysis to determine the sample size needed to detect a meaningful effect.
    3. Account for Drop-Outs: Anticipate attrition and plan for a larger sample size if necessary.

7. Step V: Study Preparation

- Study preparation is an umbrella term that refers to the items, documents, and general preparation required prior to the initiation of a medical research.
- Study preparation includes:
    1. Study proposal.
    2. Tool preparation.
    3. Timeline estimation.
    4. Ethical approval document preparation (explained in step VI).
- Study proposal preparation:
    1. A study proposal is akin to an abstract that is written PRIOR to the initiation of the study.
    2. A proposal is usually required for ethical approval, as well as grant application in the cases where external funding is required.
    3. Contents of a study proposal include the following:
        - Introduction and aim of study: This can consist of a few sentences about the subject of your research, followed by a statement of the aim of the study (what you were hoping to achieve from your research).
        - Materials and Methods: this section will include the steps taken to conduct the study (e.g. creation of a questionnaire that will be answered, patient selection criteria, inclusion and exclusion criteria), as well as the means of statistical analysis.

- Anticipated Results: this section should include the hypothesis statement of your study (e.g. this study is expected to unveil an association between electronic cigarettes smoking and chronic obstructive lung disease)
- Conclusions are not included in study proposals.

- Tool preparation:
  1. This includes the preparation of the main tool that will be used in the chosen study. Cross-sectional studies usually employ validated questionnaires that can be tested on a small sample prior to study initiation (piloting the questionnaire). Different studies employ different tools and forms. having a finalized copy of the tool is sacrosanct.
  2. This step also includes preparation of consent forms:
     - Be mindful of ensuring sample anonymity and clarifying that consent is optional and will have no consequence on treatment and behavior.
     - It is also necessary to take consent from patients if photographs are going to be taken, with disclosure of the objectives of these photographs.
     - Finally, note that taking consent from minors is not sufficient and caretaker consent is required.
     - Consent needs to be available in languages understood by the patient, and it must be documented (verbal consent is not sufficient).
  3. These tools are usually required for the ethical approval.
- Timeline estimation: estimate a timeline for study conduction (e.g. 8 weeks are needed to distribute the questionnaire of study x to the samples) as this is also required in some cases for ethical approval.

8. Step VI: Ethical Approval

- All research involving human participants and/or human tissues requires ethical approval by the standing committee for coordination of health and medical research, Ministry of Health.
- Ethical review provides protection for participants, and also helps to protect the researcher.
- By obtaining ethical approval the researcher is demonstrating that they have adhered to the accepted ethical standards of a genuine research study.
- To obtain an ethical approval the researcher should provide the following attachments sent all together:
  1. Research Protocol; Contains: Abstract, Introduction, Objective, Background, Expected outcome, and References.
  2. Research proposal.
  3. Research committee form; Signed by the primary investigator, head of department, and hospital director. In informed consent box (arrow), the researcher can write (Attachment-1) and attach the consent separately.

Ministry of Health
The Standing Committee for Coordination of Health and Medical Research

وزارة الصحة
اللجنة الدائمة لتنسيق البحوث الطبية والصحية

البيانات الرئيسية لمشروع بحث للعرض على اللجنة

تاريخ تقديم الطلب : / / رقم البحث : لسنة :

الباحث الرئيسي : | باحثون مشاركون:
هاتف نقال: فاكس :
البريد الالكتروني:
القسم / الإدارة / المستشفى / المنطقة: | مدة مشروع البحث:

عنوان البحث المقترح / Research Title:

أهداف البحث Objectives:

ملخص خطوات البحث Research Plan/ Protocol (1):

النتائج المتوقعة Expected Outcome:

إقرار الموافقة على المشاركة بالبحث (يرجى إرفاق نسخة من الإقرار باللغة العربية والإنجليزية) Informed Consent (2):
Attachment 1

إجراءات حفوق المرضى لضمان سرية المعلومات والخصوصية :
Attachment 2

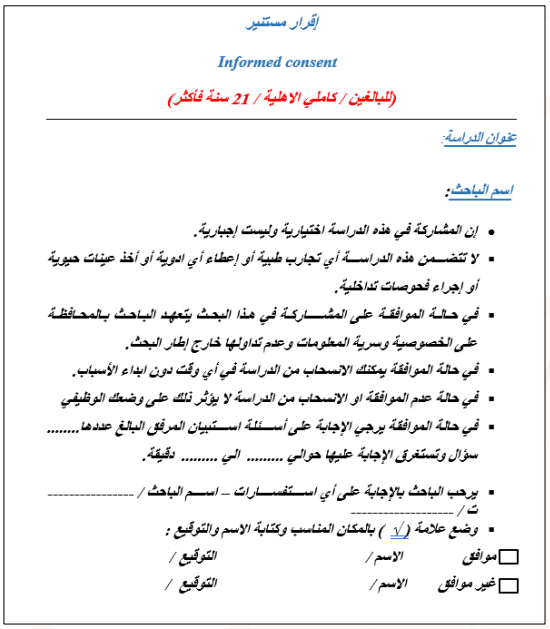
الميزانية التقديرية : | جهة التمويل الخارجية :

الموافقة على تقديم البحث

الباحث الرئيسي : | رئيس القسم: | مدير المستشفى / الإدارة :

ملاحظات:

4. Informed Consent (Attachments-2, 3)



إقرار مستنير

Informed consent

(للبالغين / كاملي الاهلية / 21 سنة فأكثر)

عنوان الدراسة:

اسم الباحث:

- إن المشاركة في هذه الدراسة اختيارية وليست إجبارية.
- لا تتضمن هذه الدراسة أي تجارب طبية أو إعطاء أي ادوية أو أخذ عينات حيوية أو إجراء فحوصات تداخلية.
- في حالة الموافقة على المشاركة في هذا البحث يتعهد الباحث بالمحافظة على الخصوصية وسرية المعلومات وعدم تداولها خارج إطار البحث.
- في حالة الموافقة يمكنك الانسحاب من الدراسة في أي وقت دون ابداء الأسباب.
- في حالة عدم الموافقة او الانسحاب من الدراسة لا يؤثر ذلك على وضعك الوظيفي
- في حالة الموافقة يرجى الإجابة على أسئلة استبيان المرفق البالغ عددها..... سؤال وتستغرق الإجابة عليها حوالي ..... الي ..... دقيقة.
- يرحب الباحث بالإجابة على أي استفسارات – اسم الباحث / ---------- ت / ----------
- وضع علامة (√) بالمكان المناسب وكتابة الاسم والتوقيع :

☐ موافق الاسم / التوقيع /

☐ غير موافق الاسم / التوقيع /

اللجنة الدائمة لتنسيق البحوث الطبية والصحية

إقرار مستنير

Informed consent

(لغير للبالغين / ناقصي الاهلية / أقل من 21 سنة)

عنوان الدراسة:

اسم الباحث:

- إن المشاركة في هذه الدراسة اختيارية وليست إجبارية.
- لا تتضمن هذه الدراسة أي تجارب طبية أو إعطاء ادوية أو أخذ عينات حيوية أو التدخل في الخطط العلاجية.
- في حالة الموافقة على المشاركة في هذا البحث يتعهد الباحث بالمحافظة على الخصوصية وسرية المعلومات وعدم تداولها خارج إطار البحث.
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- في حالة عدم الموافقة او الانسحاب من الدراسة لا يؤثر ذلك على حقك في تلقي الرعاية الصحية المقررة لك.
- في حالة الموافقة يرجى الإجابة على أسئلة استبيان المرفق البالغ عددها ---------- سؤال وتستغرق الإجابة عليها حوالي ---------- دقيقة.
- يرحب الباحث بالإجابة على أي استفسارات – اسم الباحث / ---------- ت / ----------
- وضع علامة (√) بالمكان المناسب وكتابة الاسم والتوقيع:

☐ موافق

الاسم / ..... بصفتي الولي القانوني عن / .....

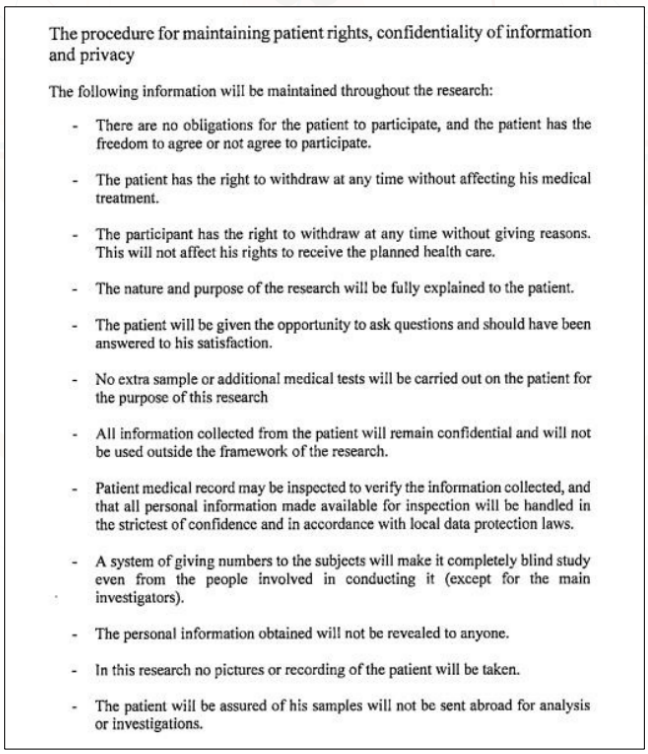
صلة القرابة / .....

☐ غير موافق

الاسم / ..... بصفتي الولي القانوني عن / .....

صلة القرابة / .....

5. Patient rights procedure to ensure confidentiality of information (Attachment-4)



The procedure for maintaining patient rights, confidentiality of information and privacy

The following information will be maintained throughout the research:

- There are no obligations for the patient to participate, and the patient has the freedom to agree or not agree to participate.
- The patient has the right to withdraw at any time without affecting his medical treatment.
- The participant has the right to withdraw at any time without giving reasons. This will not affect his rights to receive the planned health care.
- The nature and purpose of the research will be fully explained to the patient.
- The patient will be given the opportunity to ask questions and should have been answered to his satisfaction.
- No extra sample or additional medical tests will be carried out on the patient for the purpose of this research
- All information collected from the patient will remain confidential and will not be used outside the framework of the research.
- Patient medical record may be inspected to verify the information collected, and that all personal information made available for inspection will be handled in the strictest of confidence and in accordance with local data protection laws.
- A system of giving numbers to the subjects will make it completely blind study even from the people involved in conducting it (except for the main investigators).
- The personal information obtained will not be revealed to anyone.
- In this research no pictures or recording of the patient will be taken.
- The patient will be assured of his samples will not be sent abroad for analysis or investigations.

6. A paper that instates (إقرار وتعهد) from the primary investigator (Attachment-5).

إقرار وتعهد

بالمحافظة على الخصوصية سرية المعلومات

أقر أنا د./

عنوان البحث:

بأن هذا البحث هو

ولا يشمل البحث أي تداخلات مع المرضى أو إجراء أي فحوصات أو أخذ عينات حيوية أو تجارب طبية أو إعطاء أدوية.

ويتعهد الباحث بالمحافظة على الخصوصية وسرية المعلومات وعدم تداولها خارج إطار البحث والتعامل مع النتائج كأرقام وإحصائيات مجردة وعدم كتابة أسماء المشاركين بالبحث أو ما قد يدل على شخصياتهم بأي وثيقة أو مرحلة من مراحل البحث.

وهذا إقراراً مني بذلك.

مقدمته لسيادتكم

د./

- Note: for residents starting a project in which the samples are taken from external sites (students, public), the ethical approval head of department and hospital must be taken from their CURRENT site heads.

9. Step VII: Data Collection and Data Entry

- After gaining ethical approval, researchers can proceed with data collection and entry, representing the foundational stage of a research study where information is gathered systematically and recorded accurately to address the research objectives.
- Correct execution of this step ensures the availability of reliable data for analysis, facilitating the generation of meaningful insights and conclusions in dermatological research.
- **Step A: Developing a Data Collection Plan:**
- **Developing a Data Collection Plan:**
    1. Before initiating data collection, researchers must devise a comprehensive plan outlining the procedures, instruments, and timelines for gathering data.
    2. This plan should align closely with the research objectives and study design, ensuring the collection of relevant and necessary information.
- **Selecting Data Collection Methods:**
    1. The choice of data collection methods depends on the nature of the research study and the type of data required.
    2. Common methods include surveys, interviews, clinical examinations, and laboratory tests.
    3. Researchers should select methods that are appropriate, ethical, and feasible within the context of the study.
- **Ensuring Data Quality and Validity:**

1. Maintaining the quality and validity of collected data is essential to the integrity of the research findings.
2. Researchers should implement measures to minimize errors, bias, and variability during data collection, such as employing standardized protocols and training data collectors to minimize errors during data entry.
3. Researchers should regularly review data collection processes to address any discrepancies or anomalies promptly to maintain data integrity.

- **Obtaining Informed Consent:**
    1. if required for your study depending on MOH guidelines
    2. They are usually not required for retrospective analyses or chart reviews.
- **Step B: Implementing Data Collection Procedures:**
- With the data collection plan in place, researchers can proceed to implement the designated procedures for gathering information.
- This may involve administering surveys, conducting interviews, reviewing medical records, performing clinical assessments, or collecting biological samples, following established protocols and ethical and MOH's guidelines.
- **Step C: Data Entry and Documentation:**
- Once data is collected, it must be accurately recorded and entered into a structured format, a spreadsheet (e.g., Microsoft Excel or Google Sheets), for analysis (Step VIII).
- This may involve transcribing interviews, coding survey responses, or entering clinical measurements into a database.

- **EXAMPLES:**

- **Example 1**: Questionnaire-Based Study on Dermatological Knowledge and Practices
- Research Objective: To assess the knowledge, attitudes, and practices regarding sun protection behaviors among individuals aged 18-45 years visiting Asaad Ahamad Tertiary Care Center.

1. Population and Sample Selection:
    - Define the target population (e.g., adults aged 18-45 residing in urban areas).
    - Determine the sample size based on power analysis and feasibility.
    - Employ random sampling techniques to select participants from diverse demographic backgrounds.
2. Questionnaire Development:
    - Design a structured questionnaire comprising multiple-choice and Likert scale questions.
    - Include sections on demographics, sun exposure habits, sunscreen use, and knowledge about skin cancer prevention.
    - Ensure the clarity, relevance, and cultural appropriateness of questions.
3. Pilot Testing and Validation (This step can be skipped if using a validated questionnaire):
    - Conduct a pilot test with a small sample to assess the clarity and comprehensibility of the questionnaire.

- Revise the questionnaire based on feedback and conduct content validity assessment.

4. Data Collection Procedures:
    - Administer the questionnaire through face-to-face interviews, online surveys (e.g., SurveyMonkey), or mobile applications.
    - Obtain informed consent from participants before administration.
    - Ensure confidentiality and anonymity of responses.
    - Train interviewers on standardized administration procedures and ethical considerations.
    - Continuously monitor the data collection processes to ensure accuracy and completeness.

- **Example 2**: Chart Review and Retrospective Analysis of Dermatological Cases
- Research Objective: To retrospectively analyze the clinical characteristics, treatment patterns, and outcomes of patients diagnosed with psoriasis at a dermatology clinic over a five-year period.

1. Patient Selection and Case Identification:
    - Define the inclusion criteria (e.g., patients diagnosed with psoriasis between January 2016 and December 2020).
    - Acquire a list of psoriasis patients that fit these inclusion criteria through search queries in the electronic medical record or if
2. Data Extraction Variables:
    - Define the variables of interest, including demographic information (age, gender), clinical characteristics (severity of psoriasis at diagnosis, comorbidities), treatment modalities, and treatment outcomes.

- Develop a standardized data extraction form (i.e., Excel or Google sheet) to systematically capture relevant information from patient charts.

3. Data Collection Procedures:
   - Extract data from patient medical records, whether electronic (HIS) or physical files, which is unfortunately still commonly used in the ministry.
   - Ensure consistency and accuracy in data extraction by training data extractors and regularly monitoring the data entry process.
   - Adhere to regulations regarding patient privacy, confidentiality, and informed consent in accordance with the ministry's guidelines.

10. Step VIII: Data Analysis

- Data analysis is the pivotal phase of a research study, where raw data undergoes systematic scrutiny and interpretation to derive meaningful insights and draw valid conclusions.
- This crucial step transforms data into actionable knowledge, driving the research forward and contributing to the advancement of dermatological science.

1. **Data Preparation:**
    - Before diving into analysis, it is essential to ensure that the collected data is organized, cleaned, and prepared for analysis.
    - This may involve coding responses, addressing missing values, and verifying the accuracy and completeness of the dataset.
2. **Data analysis software:**
    - These software tools offer a range of features and functionalities tailored to the diverse needs of researchers in dermatology.
    - Some commonly used data analysis software include:
    - SPSS (Statistical Package for the Social Sciences):
        - SPSS is a widely-used statistical software package that offers a comprehensive range of analytical capabilities.
        - It allows researchers to perform descriptive statistics, inferential statistics, and advanced data modeling techniques.
        - SPSS provides a user-friendly interface and intuitive graphical representations of data, making it accessible to researchers with varying levels of statistical expertise.

- PSPP: A free software alternative to IBM SPSS Statistics
- R (R Statistical Computing):
    - R is a powerful open-source programming language and software environment for statistical computing and graphics.
    - It offers a vast array of packages and libraries for data analysis, covering a broad spectrum of statistical methods and techniques.
    - R is highly customizable and extensible, allowing researchers to tailor analyses to their specific research questions and requirements.
- Microsoft Excel:
    - While not specifically designed for statistical analysis, Microsoft Excel is a widely-used spreadsheet software that offers basic analytical functionalities.
    - Researchers can perform descriptive statistics, data visualization, and simple inferential analyses using built-in functions and tools.
    - Excel is accessible and familiar to many researchers, making it a popular choice for preliminary data exploration and analysis.
- When selecting a data analysis software, researchers should consider factors such as the specific analytical needs of their study, ease of use, and availability of support and training opportunities.

3. **Selecting the Appropriate Analytical Methods:**
    - The choice of analytical methods depends on the research questions, study design, and nature of the data. Studies usually employ a

combination of descriptive and inferential statistics; researchers must select methods that best address the objectives of the study.

- Descriptive Analysis:
  - Descriptive statistics provide a summary of the main characteristics of the dataset, including measures of central tendency (e.g., mean, median, mode) and dispersion (e.g., standard deviation, range).
  - This initial analysis offers insights into the distribution and variability of the data.
- Inferential Analysis:
  - Inferential statistics are used to make inferences or predictions about a population based on sample data.
  - Common techniques include hypothesis testing, regression analysis, and analysis of variance (ANOVA).
  - These methods help researchers assess relationships, test hypotheses, and identify significant findings within the data (Refer to further reading for commonly used statistical tests)

4. **Interpreting Results:**
   - Once the analysis is complete, researchers must interpret the findings in the context of the research questions and relevant literature extracted during literature review process (Step II).
   - This involves identifying patterns, trends, and relationships within the data, as well as discussing any unexpected or contradictory results.

5. **Reporting Findings:**
    - The results of the data analysis should be clearly presented in the research article, accompanied by appropriate tables, figures, and visual aids.
    - Researchers should provide sufficient detail to allow readers to understand the analysis process and evaluate the validity of the findings.
6. **Peer Review and Feedback**:
    - Seeking peer review and feedback on the data analysis process can help identify any methodological weaknesses or biases and improve the rigor and quality of the research findings.
    - Collaboration with colleagues and experts in the field can enrich the interpretation and discussion of results.
7. **Further reading:**
    - Commonly used statistical tests:

https://www.einsteinmed.edu/centers/ictr/biostatistics-epidemiology-research-design-core/berd-house/common-statistical-tests/

    - Statistical Software Websites:
        - SPSS: https://www.ibm.com/products/spss-statistics
        - PSPP: https://www.gnu.org/software/pspp/
        - R software: https://www.r-project.org/

11. Step IX: Writing Your Study

- Writing an article after completing all the required steps can be intimidating, as the written content is ultimately the part of the study that will be seen by fellow doctors, healthcare staff, as well as interested public.
- However, there is no reason to worry (even for people who are writing for the first time), as writing a paper is fairly a straightforward formula that needs to be followed.
- Things to keep note of:
  1. This is where the proposal and literature review aid in the writing of the actual paper; as the proposal introduction and methodology can be used for the paper, albeit with further elaboration and referencing.
  2. The literature review does the heavy lifting when it comes to the source of facts used in the paper. The articles found can be used, paraphrased, and used in the paper, with referencing.
- Article Write-up components are mentioned in the following pages:

1. TITLE PAGE:

- Title of article: the same title used in the proposal can be transferred here of modified. Note that you may also need to create a “working title”, which is typically a smaller version of your study title that is used for each page of the study, depending on journal rules for publication for the study
- Authors and affiliations: this area includes all authors and the supervisor for the study and the certification (Hasan Ashkanani M.D.). Classically, the supervisor of the study gets their name put last on the list, and the primary investigator (PI)’s name goes first, followed by all authors by the range of their contribution (more work equals getting the name earlier on the list). Affiliations include current working rank, place of work, institution, and country (e.g. Hasan Ashkanani, Assistant registrar, department of dermatology, Amiri Hospital, Ministry of Health, Kuwait).
- Corresponding author: The corresponding author is classically the person responsible for the study (classically the supervisor or the person who is responsible for study submission for publication). Name, affiliation, and contact information of the corresponding author should be provided.
- Number of words: this area includes the total number of words used in the entire study (separate files and title page are not included), as well as the number of words used in the abstract.
- Number of tables and figures.

2. ABSTRACT:

- The abstract of a study provides a snapshot of the study. It is available for everyone, even in subscription journal, and it is usually what is required for poster submission. An abstract is classically 250 words, but some journals have their own guides and may require less or more.
- It is sometimes recommended to write the abstract last, as it may change as you progress through the writing, especially the latter portions of the study
- An abstract must include the main components of the study: an introduction (background), materials and methods, results, discussion, and conclusion. All must be summarized; however, to fit the required word count. Case report abstracts include background, case summary, and conclusions.

3. INTRODUCTION:

- The introduction of a study (Sometimes called a background) is the first thing seen in an article. It aims to provide some background information on the topic that will be discussed and focused on during the study. Classically, background information on the region, demographic, existing literature, and evidence on the topic of focus are provided in this section of the study.
- The latter portion of the study classically shifts discussion focus from more generalized talk to specific topic-relevant paragraphs that prepare the reader for the last section of the introduction.
- The last portion of the introduction is typically dedicated to the aim of the study. In this area, a thesis statement for the research is provided. A thesis statement is the goal of the research, and it must be specific to the study, topic, and sample "e.g. this study aims to assess the epidemiology of adult congenital heart disease among the general population in Kuwait".

4. MATERIALS AND METHODS:

- This part includes a detailed description of the tools that were chosen back in Step V. the description has to be clear and thorough.
- If it is a questionnaire, the number of questions and mode of distribution have to be mentioned.
- Sample inclusion and exclusion criteria must be mentioned as well.
- Study pilots are included in this section, and ethical approval must me noted as well.
- Finally, time frame for sample collection is noted here, and the mode of statistical should be mentioned.

5. RESULTS:

- The result section of the study is where the findings are written.
- These findings are mentioned based on the result of the data collection, data entry, and data analysis.
- Results usually start with the number of samples collected, with the response rate written in percentage:
    - (total sample / people who accepted to participate x 100).
- The second thing mentioned is sample demographics (age, gender, nationality, etc.).
- The third part is the meat of the study, which is the content results found based on statistical analysis. Correlation between questions or findings with demographics or other findings is a useful method to find additional data (e.g. among people with more than 5 flare-ups of psoriasis a year, females were noted to have a higher incidence than males).
- Statistical significance must be mentioned here (even if it is not statistically significant, you can mention it in the study but note that it is not statistically significant (P-Value < 0.05)).

6. DISCUSSION:

- The discussion of a study is the elaboration and reasoning region for the result section. Findings mentioned in the result section are mentioned here but with further elaborations.
- Congruence or differences between the findings of your study and common literature are mentioned in this section, and studies used for comparison are referenced. (e.g. this study found that females in Kuwait have a higher incidence of breast cancer, which matches the findings in a similar study conducted in Spain (reference)).
- Hypotheses and possible explanation behind the findings are also written here but it is useful to mention that it is a possibility (e.g. this study found that people in Kuwait have a lower incidence of basal cell carcinoma of the skin, which COULD BE due to reduced sun exposure and outdoor activities).

7. CONCLUSION:

- This is essentially the final part of your writing.
- A summary statement usually starts the conclusion region. It includes an important statement or two about the background.
- Following the summary statement is the what the study aimed to achieve.
- Next, a summary of the KEY findings is mentioned.
- Finally, a closing statement is written, with any recommendations for practice change or further research needed based on this study.

8. OTHER POSSIBLE ITEMS:

- Strengths and Limitations: strengths are unique things in the study that makes it stand above the rest (e.g. this is the FIRST study in the gulf region that identifies causes of x). on the other hand, limitations are weaknesses identified in the study (e.g. small sample size, sample of convenience, small follow-up period, small response rate, etc.).
- Acknowledgements: this area is where you acknowledge help from people or sectors that were not included in authorship.
- Conflicts of interest: mentioned here if there are financial gains or other sorts of conflict.
- Funding: mentioned here.
- Author contributions: the contribution of each author by specifics can be mentioned here (e.g. hasan Ashkanani wrote the introduction).
- Data Availability Statement: Usually written as the following: Data is available with the corresponding author and can be obtained upon request.

9. REFERENCES:

- This section includes referencing ALL the studies that were used in the creation of the article.
- It is advisable to create your references as you write your paper.
- Referencing style is variable, but it can be changed easily.
- As a general consensus, academic papers use the Harvard and APA style of referencing.
- References can be added by using programs like EndNote.
- You can enter your article that you are referencing to the program, and then you can insert the reference from the “References” tab in Microsoft Word.
- It is advisable to insert the references in order of usage (earlier references used in the introduction section are referenced higher up (earlier)).
- References used more than once are only entered once in the references section.

10. APPENDICES:

- Appendices are used depending on the journal, but they generally include:
    - Tables
    - Figures
    - Photographs
    - Tools used for the paper (questionnaires, consent forms).
- The items must have titles and description, and they are put in the same order they are mentioned in the article for each item. (tables are all put first, but table order is dependable on the study

- Special formats and steps are taken for **CASE REPORTS AND SERIES**, and these include:

1. **Introduction:**
   - Same as the introduction used in a normal article, but with the change in the aim of study
2. **Case Summary:**
   - This section includes a full summary of the case that is intended for the report. A regular case summary includes full history, physical examination, laboratory tests, imaging results, photographs, and treatment description. Note that it is important to highlight the specific rarity, finding, or intervention that makes this case worthy of a report.
   - Case series follow the same case summary format, albeit multiple times.
3. **Conclusion**
   - This is essentially the final part of your writing.
   - A summary statement usually starts the conclusion region. It includes an important statement or two about the background and condition.
   - Next, a summary of the KEY findings in your case or cases is written.

12. Step X: Publishing Your Study

- Publishing your study is usually the last step in research, and it means sharing your study for the public and scientific community to read and learn from. It is a high academic feat as a medical doctor to have published studies, as it means that you are taking a role in enriching medical literature and possibly even changing the practice in the field.
- Start first by understanding Journal Types and Selection Criteria:
    1. Specialty vs. General: Determine if your study is best suited for a specialty journal that aligns with your research niche or a more general medical journal with a wider readership.
    2. Impact Factor and Audience: Consider the journal's impact factor, which indicates the frequency with which articles are cited, and identify who the primary audience is (e.g., clinicians, researchers, policymakers).
    3. Open-Access vs. Subscription-Based: Reflect on open-access journals that make articles freely available to all readers, versus subscription-based ones, which may have a broader reputation but limited access.
    4. Relevance and Precedence: Analyze previous articles published in the journal to ensure relevance to your work and assess the precedence of topics similar to your research.
    5. Peer Review Process: Familiarize yourself with the journal's peer-review process: double-blind, single-blind, or open review.
    6. Publication Speed and Frequency: Evaluate how quickly articles are published after acceptance and consider the frequency of journal issues.

- Preparation for Submission:
    1. Formatting Guidelines: Carefully read the journal's author guidelines for formatting requirements including the structure of abstracts, manuscript style, reference format, and figure/table specifications.
    2. Cover Letter: Craft a compelling cover letter that introduces your study, explains its significance, states why the journal fits your work, and discloses any potential conflicts of interest.
    3. Manuscript Components: Ensure the manuscript includes all required sections—abstract, introduction, methods, results, discussion, conclusions, references, figures and tables, and any supplementary material.
        - The title: Be specific and to the point.
        - The abstract: Make it easily understood without the reader having to read the whole article. This section is a mini summary of the main sections in your paper. This section is very short and to the point. Most journal articles ask for the abstract to be between 240-260 words. Here are some tips on how to write it:
            - Must be written in past tense at it describes work done.
            - Never include information not present in the paper.
            - You don't need to put citations in the abstract.
            - Some authors will write the abstract after writing the manuscript.
        - Keywords: keywords are used by abstracting and indexing services such as PubMed. They are the labels of your manuscript, which makes it searchable online by other researchers. Include words or phrases (usually 4-8) that are closely related to your topic.

- Introduction: It should introduce the problem and solution. Also, state what you hope to achieve with your research. Make the rationale of your study clear and include references that provide the most relevant background to your study. Don't forget to briefly state the methods of your investigations and results at the end of your introduction. Any specialized terms can also be defined here.
- Methods: To provide the reader with enough information to be able to judge whether the study is valid and reproducible.
- Results: Display them in a comprehensible way. You should use subheadings as well as illustrations such as figures graphs tables and photos, as appropriate.
- Discussion: State how the results relate to the study's aims and hypothesis and how the findings relate to those of other studies. Explain all possible interpretation of your findings and the study's limitation.
- Conclusion: It should be a summary of what you have already written and answer any unresolved questions.
- Acknowledgments and ethical statements: It is important to acknowledge anyone who has helped you with your paper including researchers who supplied materials over agents.
- References: Remember to cite the main scientific publications

4. Ethical Considerations: Verify that ethical approvals and patient consents are appropriately mentioned.
5. Authorship Acknowledgement: Confirm the authorship list, ensuring that all contributors fulfilling the authorship criteria are credited.

- Submission Process:
    1. Online Submission System: Most journals use an online submission system where you will create an account, fill in author details, upload the manuscript files, and possibly suggest potential reviewers.
    2. Tracking Manuscript Status: Utilize the submission system to track the review status of your manuscript.
    3. Responding to Reviews: Prepare to carefully address reviewer comments, either making changes to the manuscript or providing a well-argued rebuttal to each point.
    4. Revisions and Resubmission: Revise the paper according to the journal's and reviewers' comments and resubmit within the stipulated time frame if required.
    5. Acceptance: Upon acceptance, review proofs for any typesetting errors and return corrections quickly.
    6. Promotion: After publication, promote your article through professional networks and social media to reach a broader audience.
    7. By adhering to these considerations and processes, medical residents will increase their chances of successfully publishing their scholarly work, thereby contributing valuable knowledge to the medical community.

13. Step XI (Optional): Poster Preparation

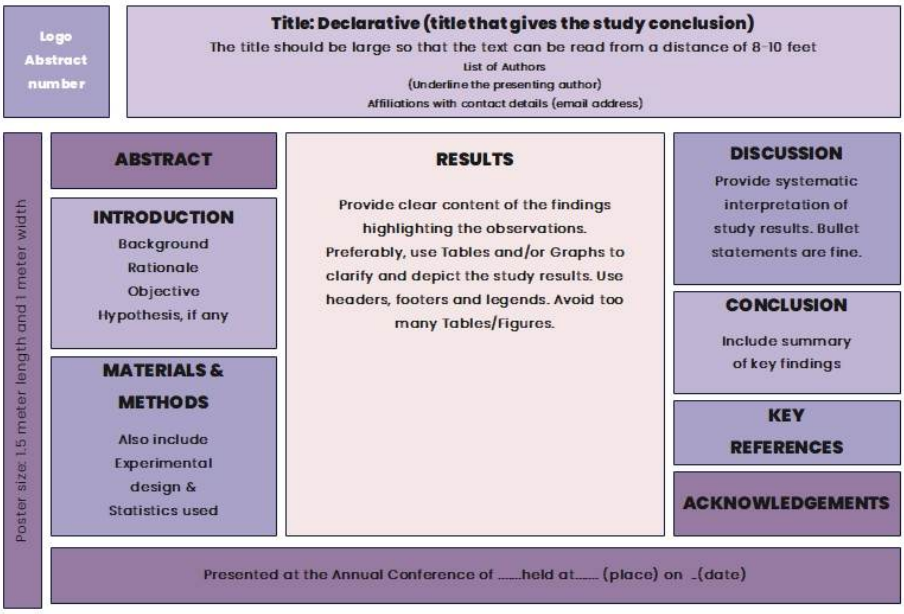
- A scientific poster is a popular method of presenting research findings succinctly at meetings and conferences.
- On a poster, which is usually designed on a computer using a program like Microsoft PowerPoint, you summarize your research project using a mix of text and diagrams/images.
- You will then possibly need to get your poster printed and take it to the meeting where it is to be presented, depending on the meeting and their rules.
- Understanding the Purpose:
    1. Identify the core message of your research (condense the aims, methods, results and conclusions of your research into a portable form of presentation.
    2. It also allows interested peers to understand your research in your absence, simply by reading through your poster.
- Before making a poster, start by checking what the conference organizers want. They will usually specify what format your poster should be in for their conference e.g. A1 portrait or A0 landscape. It is important to adhere to these specifications as organizers may refuse to let you put your poster up if it does not match their specifications.
- How to make a poster?
    1. In PowerPoint, you can make the poster on a single slide. You can set the slide according to the specification by clicking on the 'Design' tab and clicking on Page setup. If you need to make A0, A1, or A2 posters, you will need to enter the length and width measurements manually.

2. Now that you have the correct size and orientation, you can think about the layout that you want. At their simplest, posters should contain a title, a list of author names and all the sections you might expect to see in an abstract or a standard scientific paper: background, aims, method, results and conclusions.
3. But a scientific poster is more than simply a condensed version of a paper. The poster will need to catch the reader's eye, be laid out in an intuitive way, contain enough detail to leave the reader with a sense of having understood the subject yet not excessive text so as to bore them and have diagrams to allow the reader to visualize concepts.
4. Think carefully about how you want to arrange the sections of your poster: will your information flow better if you arrange it horizontally (i.e. in rows) or vertically (i.e. in columns)? Where will the figures go?
5. In order to allow people to skim through your poster and get an idea of your research, text should be kept to a minimum – summarizing what you want to say into a few words can be very difficult, especially if you think excluding certain crucial pieces of information may leave readers confused about the subject. However, your figures should help clarify the subject – what the text doesn't specify, the figure should, and vice-versa.

- Poster content is similar to the content outline of the study, and it includes:
    1. Background/Introduction: This can consist of a few sentences about the subject of your research. Consider including a figure or two explaining your background in pictorial form.

2. Aim/Objective: This is probably the most important part of the poster as it will tell the reader what you were hoping to achieve from your research. Make this as clear as possible.
3. Method: This section may often take up a lot of precious space, especially if you have to describe novel tools or tests. At the very least, the process of your project (i.e. the sequence of events, number of trials etc.) can be summarized in a flow diagram – this may take some effort to design but it will save you space and may actually be easier on the eyes.
4. Results: This is where you would include any graphs or results tables. All graphs, including the axes, need to be adequately labelled. It may also be a good idea to redo your graphs in Microsoft Excel or any other program that lets you keep the background of graphs clear and gives you the option of removing grid lines which can be a hindrance when trying to interpret a graph. p-values that are relevant to the graphs can be included directly on graphs (as a text box) rather than within the caption or elsewhere, in order to make it easier for the reader to spot them.
5. Conclusion and implications: This should typically be one or two sentences. When presenting your poster, you should spend some time explaining the implications of your findings to the listeners as your ideas may help change practice or generate further research. You might even consider including a section on the limitations of your study, but again this will take up space and are probably best included in the verbal discussion with the listener that you will have whilst standing next to your poster.

- After you have completed a draft of the poster rehearse explaining your poster to different audiences and ask peers or mentors to review your poster and provide feedback.
- Prepare to present by being ready to provide a 3-5-minute synopsis of your work. Also, prepare to answer questions about any aspect of your research and engage with viewers; invite discussion and feedback.
- Finally, print your poster on durable, quality paper. You could ask the printer to be either laminated and/ or encapsulated. Lamination adds a plastic sheet to the poster giving it a shinning effect. There are two types of laminations, matte and gloss. Matte finish is useful if your poster has images that need to look clear. There is less of a glare; however, the poster as a whole may look 'dull'. Gloss finish is shinier (similar to magazine paper) and may be better for fine detail.



14. Appendix

- This section includes the papers you may need for paper creation, including:
    1. Ministry of Health, Kuwait - Ethical approval papers.
    2. Research proposal sample.
    3. Sample study that was already published (Cohort).

اللجنة الدائمة لتنسيق البحوث الطبية والصحية
إقرار مستنير
Informed consent
(لغير للبالغين / ناقصي الاهلية / أقل من 21 سنة)

عنوان الدراسة:

اسم الباحث:

- **إن المشاركة في هذه الدراسة اختيارية وليست إجبارية.**
- **لا تتضـــمن هذه الدراســـة أي تجارب طبية أو إعطاء ادوية أو أخذ عينات حيوية أو التدخل في الخطط العلاجية.**
- **في حـالـة الموافقـة على المشـــاركـة في هذا البحث يتعهد الباحث بالمحـافظـة على الخصوصية وسرية المعلومات وعدم تداولها خارج إطار البحث.**
- **في حالة الموافقة يمكنك الانسحاب من الدراسة في أي وقت دون ابداء الأسباب.**
- **في حالة عدم الموافقة او الانســـحاب من الدراســـة لا يؤثر ذلك على حقك في تلقي الرعاية الصحية المقررة لك.**
- **في حالة الموافقة يرجي الإجابة على أسئلة استبيان المرفق البالغ عددها --------- سؤال وتستغرق الإجابة عليها حوالي ---------- دقيقة.**
- **يرحب الباحث بالإجابة على أي اســـتفســـارات – اســـم الباحث / ---------- ت / ----------**
- **وضع علامة (√) بالمكان المناسب وكتابة الاسم والتوقيع:**

☐ **موافق**

الاسم / ..... بصفتي الولي القانوني عن / .....
صلة القرابة / .....

☐ **غير موافق**

الاسم / ..... بصفتي الولي القانوني عن / .....
صلة القرابة / .....

إقرار مستنير

Informed consent

(للبالغين / كاملي الاهلية / 21 سنة فأكثر)

عنوان الدراسة:

اسم الباحث:

- ***إن المشاركة في هذه الدراسة اختيارية وليست إجبارية.***
- ***لا تتضمن هذه الدراسة أي تجارب طبية أو إعطاء أي ادوية أو أخذ عينات حيوية أو إجراء فحوصات تداخلية.***
- ***في حالة الموافقة على المشاركة في هذا البحث يتعهد الباحث بالمحافظة على الخصوصية وسرية المعلومات وعدم تداولها خارج إطار البحث.***
- ***في حالة الموافقة يمكنك الانسحاب من الدراسة في أي وقت دون ابداء الأسباب.***
- ***في حالة عدم الموافقة او الانسحاب من الدراسة لا يؤثر ذلك على وضعك الوظيفي***
- ***في حالة الموافقة يرجي الإجابة على أسئلة استبيان المرفق البالغ عددها..... سؤال وتستغرق الإجابة عليها حوالي ..... الي ..... دقيقة.***
- ***يرحب الباحث بالإجابة على أي استفسارات – اسم الباحث / ---------- ت / ----------***
- ***وضع علامة (√) بالمكان المناسب وكتابة الاسم والتوقيع :***

☐ ***موافق*** ***الاسم /*** ***التوقيع /***

☐ ***غير موافق*** ***الاسم /*** ***التوقيع /***

إقرار وتعهد

بالمحافظة على الخصوصية سرية المعلومات

أقر أنا د./

عنوان البحث:

بأن هذا البحث هو

ولا يشمل البحث أي تداخلات مع المرضى أو إجراء أي فحوصات أو أخذ عينات حيوية أو تجارب طبية أو إعطاء أدوية.

ويتعهد الباحث بالمحافظة على الخصوصية وسرية المعلومات وعدم تداولها خارج إطار البحث والتعامل مع النتائج كأرقام وإحصائيات مجردة وعدم كتابة أسماء المشاركين بالبحث أو ما قد يدل على شخصياتهم بأي وثيقة أو مرحلة من مراحل البحث.

وهذا إقراراً مني بذلك.

مقدمته لسيادتكم

د./

INFORMED CONSENT CHECKLIST	
A statement that the study involves research.	
An explanation of the purposes of the research.	
An explanation of the expected duration of the participant's participation.	
A description of the procedures to be followed.	
Identification of procedures that are experimental. (May be omitted if there are none.)	
A description of any reasonably foreseeable risks or discomforts to the participant. (May be omitted if there are none.)	
A description of any benefits to the participant or to others, which may reasonably be expected from the research. (May be omitted if there are none.)	
A disclosure of appropriate alternative procedures or courses of treatment, if any, that may be advantageous to the participant. (May be omitted if there are none.)	
A statement describing the extent, if any, to which confidentiality of records identifying the participant will be maintained. (May be omitted if confidentiality will not be maintained.)	
A statement that notes the possibility that the Food and Drug Administration may inspect the records (May be omitted for research that is not FDA-regulated.)	
An explanation as to whether compensation is available if injury occurs. (May be omitted if the research involves no more than minimal risk.)	
If compensation is available when injury occurs, an explanation as to what it consists of or where further information may be obtained. (May be omitted if the research involves no more than minimal risk.)	
An explanation of whom to contact for answers to pertinent questions about the research.	
An explanation of whom to contact for answers to pertinent questions about the research participants' rights	
An explanation of whom to contact in the event of a research-related injury to the participant. (Note: May not be omitted just because the research involves no more than minimal risk.)	
A statement that participation is voluntary.	
A statement that refusal to participate will involve no penalty or loss of benefits to which participant is otherwise entitled.	
A statement that the participant can discontinue participation at any time without penalty or loss of benefits to which the participant is otherwise entitled.	
A statement that the particular treatment or procedure may involve risks to the participant, which are currently unforeseeable. (Look for when research involves investigational drugs/devices, novel procedures involving risk, or where a goal of the research is to define safety.)	
A statement that if the participant is or becomes pregnant, the particular treatment or procedure may involve risks to the embryo or fetus, which are currently unforeseeable. (Look for when the research involves pregnant women or women of childbearing potential, and the effect of the procedures have not been evaluated in pregnancy or a goal of the	
The approximate number of participants involved in the study	
Anticipated circumstances under which the participant's participation may be terminated by the investigator without regard to the participant's consent.	
Any additional costs to the participant that may result from participation in the research.	
The consequences of a participant's decision to withdraw from the research and procedures for orderly termination of participation by the participant	
A statement that significant new findings developed during the course of the research which may relate to the participant's willingness to continue participation will be provided to the participant.	
The amount and schedule of all payments to the participant	

Ministry of Health
The Standing Committee
for Coordination of
Health and Medical

وزارة الصحة
اللجنة الدائمة لتنسيق
البحوث الطبية والصحية

البيانات الرئيسية لمشروع بحث للعرض على اللجنة

تاريخ تقديم الطلب:	/ /	رقم البحث :	لسنة :
الباحث الرئيسي: Principle Investigators		باحثون مشاركون: Co- Investigators	
القسم / الإدارة / المستشفى / المنطقة: Dept./Hospital/ Health Region			
التليفون: Tel:		الايميل: Email :	
الجهات التي سيتم اجراء البحث بها:		مدة مشروع البحث: Expected length of the Study	

عنوان البحث المقترح / Research Title:

أهداف البحث Objectives:

ملخص خطوات البحث Research Plan/ Protocol (1):

النتائج المتوقعة Expected Outcome:

إقرار الموافقة على المشاركة بالبحث (يرجي إرفاق نسخة من الإقرار باللغة العربية والإنجليزية) Informed Consent (2):
(Informed Consent (please submit a copy in Arabic and English)

إجراءات حقوق المرضي لضمان سرية المعلومات والخصوصية:
and patient Privacy an rights ion Steps followed to ensure confidenialty of Informed

الميزانية التقديرية: Expected Budget		جهة التمويل الخارجية: Source of Fund

الموافقة على تقديم البحث

الباحث الرئيسي : Primary Investigator	رئيس القسم: Chair of Dept.	مدير المستشفى / الإدارة : Director

- يتم تقديم النموذج إلى / مكتب الوكيل المساعد لشئون التخطيط والجودة / رئيس اللجنة - ويرفق به الوثائق المطلوبة (خطة وبروتوكول البحث – نماذج الإقرارات - والمعلومات المطلوبة) .
- سكرتير اللجنة – السيد / الحسن خميس عبد الله / ت / 90069869 / hkhamis@moh.gov.kw
والسيد / خليفة الخطيب – ت / 99202337 / kkhalifa@moh.gov.kw بمكتب الاعلام الصحي – بوزارة الصحة / الدور الأرضي .
- مرفق تعميم من السيد / وكيل الوزارة - رقم 156 لسنة 2012

Radiology in the Undergraduate Medical Curriculum: A Student Perspective

Ashkanani H, AlDallal Y, Gupta R

Introduction and Background: All practitioners are expected to interact with radiologists during their clinical practice, as radiology provides significant imaging information that guides the clinical decision-making and can even be used for treatment [1]. Despite the significant importance of radiology, articles suggest that new medical graduates exhibit a minimal level of radiology knowledge with approximately half of graduates not knowing the risks of common investigations or how to select the appropriate clinical investigation [2,3]. This could possibly result in potential risk to patients in clinical practice. Internationally, hours spent in the radiology training in the undergraduate level vary dramatically, as formal radiology education is not offered in all undergraduate medical programs, and it is only offered as an elective instead [1]. However, in Kuwait University, which follows a seven-year mixed basic sciences and clinical program, with the first four years being offered at the preclinical and basic science level and the other three as clinical years, students spend only one week in the radiology rotation [4]. This study aims to assess Kuwait University medical students' satisfaction with the radiology rotation and their confidence level in ordering appropriate imaging studies and making common diagnoses. Also, this study aims to assess students' knowledge regarding the basic radiological principles, as well as their recommendation to improve the teaching process.

Methods: A review board–approved survey will be used to ask medical students starting from their fourth academic year the following questions: 1) extent of medical school training for ordering and interpreting imaging studies, 2) confidence levels in ordering

appropriate imaging studies and making common/emergent diagnoses, and 3) rating the importance of radiologic interpretation [5]. Respondents will also be asked to submit ideas for medical school teaching topics deemed most useful.

Anticipated Results: Students, regardless of requirements, are anticipated to think there is value in having radiology as a regular aspect of a medical school curriculum. Medical schools should consider ways of incorporating radiology more into their clinical curriculum.

frontiers in Neurology

ORIGINAL RESEARCH
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Onabotulinumtoxin A Improves Psychological Aspects in Chronic Migraine Patients

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Background: Chronic migraine (CM) affects 5.4% of the Kuwaiti population. It is associated with significant headache-related disability, psychiatric comorbidity and reduced quality of life. The aim of this study is to assess the efficacy of Onabotulinumtoxin A on psychological aspects of chronic migraine patients.

Methods: This prospective study over 36 months included chronic migraine patients in a tertiary headache center. Eligible patients met International Classification of Headache Disorders disorders-third edition, beta version (ICHD-III) revision criteria for chronic migraine. Patients with history of psychiatric or medical problems other than migraine disorders were excluded. Patients who received less than 4 injections cycles of Onabotulinumtoxin A were excluded. Identified patients received 155 units of Onabotulinumtoxin A quarterly according to the Phase III Research Evaluating Migraine Prophylaxis Therapy Trail (PREEMPT) protocol. Quality of life, the seven-item Generalized Anxiety Disorder (GAD-7) scores, the nine-item Patient Health Questionnaire (PHQ9), and the Pittsburgh Sleep Quality Index (PSQI) were collected before injection and at the end of the study. Mean comparison tests were performed using the independent sample *t*-test to assess the effects of Onabotulinumtoxin A on quality of life and comorbid symptoms of anxiety, depression, and quality of sleep.

Results: The study identified 131 chronic migraine patients with a mean age of 44.92 years, mean disease duration of 12.20 years and a mean treatment sessions of 7.58. In their last visit, most of our sample showed improvement in quality of life (81%), GAD-7 (81%), PHQ9 (79%), and PSQ1 (76%). The mean score of patient satisfaction was 7.21. Onabotulinumtoxin A treatment for CM improved quality of life significantly (72.92 vs. 103.62; $P < 0.0001$). It was also associated with significant reduction in anxiety [GAD-7 (12.00 vs. 6.61; $P < 0.0001$)] and depression [PHQ-9 (17.91 vs. 12.52; $P < 0.0001$)] scores, as well as reduced difficulty in sleeping [PSQI (12.60 vs. 6.66; $P < 0.0001$)] at the last visit.

Conclusion: Prophylactic Onabotulinumtoxin A treatment for CM was associated with significant improvement of quality of life, reduction in symptoms of anxiety and depression, as well as improved symptoms of poor sleep.

Keywords: Onabotulinumtoxin A, chronic migraine, depression, anxiety, sleep disturbance

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BACKGROUND

Migraine, a primary type of headache, is a common disabling disorder that can be divided into episodic and chronic migraine (1). The global prevalence of migraine is 14.4%, for females, and 9.8% for males (2). Global studies show that ∼1.4–2.2% of the world's population have been diagnosed with chronic migraine (2). Comparatively, the 1-year prevalence of migraine in Kuwait was 23%, which is significantly higher (3). According to the latest Global Burden of Disease Study, headaches, including migraines, ranked second in the leading causes of disability, showing the large burden of the disorder (4). Migraine majorly affects the everyday lives of its sufferers, negatively affecting productivity, and even schooling (5). This burden is also increased by the comorbid psychiatric conditions that occur in association with it, including depression, anxiety, and sleep disorders. Large scale, population-based studies showed that patients with migraine are 2.2–4.0 times more likely to have depression (6). Moreover, in those who have episodic migraines, depression was associated with an increased risk of developing chronic migraine (7). In addition, the diagnosis of generalized anxiety disorder was significantly more prevalent in migraineurs than in those without migraine (8). Generalized anxiety disorder is often comorbid with major depressive disorder (MDD) and both of them increase the burden of migraine (8). Therefore, patients with migraine and psychiatric comorbidities may benefit from preventive therapy to reduce the attacks.

Sleep has also been demonstrated to have a clear relationship with migraine. Chronic migraine patients (CM) reported shorter nightly sleep periods than those with episodic migraine, and they were more likely to exhibit trouble initiating sleep, staying asleep, and sleep triggering headache. Also, complaints of those insomnia symptoms were at least three-fold greater in those patients than the general population (9). This shows the importance of management in migraine patients in the hope of decreasing this socioeconomic and medical burden. Therefore, patients with migraine and psychiatric comorbidities may benefit from preventive therapy to reduce the attacks.

Onabotulinumtoxin A was approved as a prophylactic therapy in adult patients with chronic migraine by the United State Food and Drug Administration (FDA) in 2010 (10). Onabotulinumtoxin A has been proven to reduce not only headache frequency but also the symptoms of depression, anxiety, as well as poor sleep quality in migraine patients (11).

While Onabotulinumtoxin A is known to cause muscle paralysis, the exact mechanism by which it relieves chronic migraine is not clear as of yet. However, some evidence suggests it does so by reducing local nerve sensitization by local inhibition of neuropeptide release, thus resulting in an indirect reduction of central sensitization (12). The neuropeptide calcitonin gene-related peptide (CGRP), which is known to be a major player in migraine, might be involved in regulating sleep maintenance at night (13, 14). Therefore, Onabotulinumtoxin A treatment may help to improve sleep in migraine patients by repressing CGRP from activated sensory neurons and by directly decreasing the amount of CGRP released from trigeminal neurons (15).

Although the socioeconomic burden of migraine in the Kuwaiti population was previously studied (3), no study to date has assessed the psychological aspects as mood and sleep suffering from migraine in patients in Kuwait. Therefore, this study aims to show the effect of treatment on improvement of mood and sleep in chronic migraine patients who received Onabotulinumtoxin A injections.

METHOD

This prospective, questionnaire-based study was conducted in a specialized headache clinic in a tertiary hospital in Kuwait. The study started on 1st October 2016 until 30 September 2019. The study population included both male and female patients aged 18–65 years who are diagnosed with CM with or without medication over use headache (MOH). Diagnoses were confirmed by headache specialist according to International Classification of Headache Disorders III (ICHD-III) (1). The study excluded patients with psychiatric disorders or chronic medical problems.

Patients with a diagnosis of another headache disorder, previous use of any Onabotulinumtoxin A for treatment of any headache (at any time) or for any other reason in the last year, pregnant or breast-feeding patients, and patients who did not complete at least three treatment cycles were excluded from the study. In addition, patients who had psychiatric comorbidities, history of previous psychiatric diseases, other migraine comorbidities, such as hypertension, obesity, or smoking, or those taking other medications from Onabotulinumtoxin A for migraine were not eligible for inclusion in the study. Study excluded patients who are on tricyclic antidepressant or selective serotonin reuptake inhibitors as prophylactic treatment for chronic migraine. Also, patients who received <4 injections cycles of Onabotulinumtoxin A were excluded.

Patients were injected intramuscularly with Onabotulinumtoxin A according to the PREEMPT protocol, 155 units divided into 31 injection sites around the head and neck, with sessions occurring in every 3 months (10).

A total of four questionnaires were used to interview patients in order to collect the data for the study. The questionnaires used in the study include The Quality of Life (QOL) (16), Generalized Anxiety Disorder-7 (GAD-7) (17) The Pittsburgh Sleep Quality Index (PSQI) (18) and The Patient Health Questionnaire-9 (PHQ-9) questionnaires (19).

Outcomes measured included change in PHQ-9, GAD-7, PSQI, and QOL from baseline. The patients were asked to answer above mentioned questionnaires twice; initially, prior to their first session in treatment, and the second after at the end of study

Abbreviations: CGRP, Calcitonin gene-related peptide; CM, Chronic migraine; DSM-5, Diagnostic and Statistical Manual of Mental Disorders; FDA, Food and Drug Administration; ICHD-III, International Classification of Headache Disorders III; MDD, Major depressive disorder; MOH, Medication over use headache; PHQ9, Patient Health Questionnaire; PREEMPT, Phase III Research Evaluating Migraine Prophylaxis Therapy Trail; QOL, Quality of Life; GAD-7, Seven-item Generalized Anxiety Disorder; PSQI, The Pittsburgh Sleep Quality Index.

if they completed at least four cycle of medications. The changes in the answers were compared to determine the effectiveness of the Onabotulinumtoxin A treatment.

Improvement by ≥1 in severity category in the PHQ-9 or GAD-7 score from baseline was considered to be a clinically meaningful improvement (20, 21). On the other hand, a reduction by ≥3-point in the total PSQI score was considered a clinically meaningful improvement (22). Treatment satisfaction was assessed by numeric scale, in which 0 meant no satisfaction at all and 10 means the patient was fully satisfied.

This study was carried out in accordance with the ethical guidelines of Kuwait Ministry of Health. The protocol was approved by the ethical committee of Ibn Sina hospital. All subjects gave a written informed consent in accordance with the Declaration of Helsinki. The study was performed in observation of the latest version of the declaration of Helsinki (23), and all data was anonymous and protected in accordance with the ethical guidelines of the Council for International Organizations of Medical Sciences (24).

Statistical analyses were performed with IBM SPSS Statistics 25.0 software for Mac (SPSS Inc., Chicago, IL, USA). All continuous variables were expressed as means, whereas categorical ones were expressed as proportions and percentages. Paired sample *t*-test was used to compare between PHQ-9, GAD-7, PSQI, and QOL before and after treatment with Onabotulinumtoxin A. Pearson's correlations were performed for metric and ordinal variables between adverse events and quality of life. A significant difference was set to be at $p < 0.05$.

RESULTS

This cohort study included 139 CM patients. The eligible patients were131. **Table 1** shows demographic and clinical characteristics of our cohort. The participants had mean age of 44.92 years, mean disease duration 12.20 years and a mean number of sessions 8. At the end of the study, most of the patients showed a significant improvement in the quality of life (81%), GAD-7 (81%), PHQ9 (79%), and PSQ1 (76%).

The mean score of patient satisfaction was 7.21. Onabotulinumtoxin A treatment for CM improved the quality of life significantly (72.92 vs. 103.62; $P < 0.0001$). It was also associated with significant reduction in the generalized anxiety scores (GAD-7) (12.0 vs. 6.6; $P < 0.0001$); depression scores (PHQ-9) (17.9 vs. 12.52; $P < 0.0001$) as well as sleep difficulty (PSQI) (12.6 vs. 6.7; $P < 0.0001$) at last visit (**Table 2**, **Figure 1**).

Our results did not conclude any significant difference among males and females regarding treatment satisfaction or improvement of psychological aspects (**Table 3**).

We reported significant correlation between satisfaction for treatment and improvement of psychological aspects. However, we did not record any significant correlation between age, gender, education years, disease duration, education, and improvement of psychological aspects (**Table 4**). This means that improvement of psychological aspects in CM patients lead to treatment satisfaction regardless age, gender, disease duration, or education.

TABLE 1 | Demographic and clinical characteristics of chronic migraine patients ($N = 131$).

Variable	Mean ± SD/No (%)
Age	44.92 ± 9.47
Range	23–65
Gender	
• Female	116 (88.5)
• Male	15 (11.5)
Disease duration in years	12.20 ± 10.10
Number of sessions	7.58 ± 3.36
Education level	
• Less than 12 years education	7 (5.3)
• 12 years education	14 (9.9)
• More than 12 years education	11 (84.7)
Improvement of psychological aspects with Onabotulinumtoxin A	
• QOL	81 (61.8)
• GAD-7	81 (61.8)
• PHQ9	79 (60.3)
• PSQI	76 (58)
Treatment satisfaction	7.21 ± 2.21

QOL, Quality of Life; GAD-7, Seven-item Generalized Anxiety Disorder; PHQ9, Patient Health Questionnaire; PSQI, The Pittsburgh Sleep Quality Index.

TABLE 2 | Impact of Onabotulinumtoxin A on psychological aspect in chronic migraine patients ($N = 113$).

Variables	Before treatment Mean ± SD	After treatment Mean ± SD	*P*-Value
QOL	72.92 ± 17.34	103.62 ± 15.62	0.0001*
GAD-7	12.00 ± 4.40	6.61 ± 4.40	0.0001*
PHQ9	17.91 ± 8.43	12.52 ± 8.77	0.0001*
PSQI	12.60 ± 5.66	6.66 ± 5.04	0.0001*

*QOL, Quality of Life; GAD-7, Seven-item Generalized Anxiety Disorder; PHQ9, Patient Health Questionnaire; PSQI, The Pittsburgh Sleep Quality Index. *Statistically significant.*

Few patients reported adverse effects related to Onabotulinumtoxin A treatment, which included neck pain and stiffness 3 (2.7%), lateral eyebrow elevation 2 (1.8%), ptosis 5 (4.44%). However, there was no significant correlation with these adverse events and quality of life after treatment ($P < 0.62$; $r = 0.044$). They were mild and irreversible.

DISCUSSION

Migraine is a common neurological disease that can be very disabling on the patients and their families. It is associated with reduced quality of life and other psychiatric comorbidities (25). Migraine is primarily managed through three approaches: lifestyle and behavioral modification, acute therapy, and prophylactic therapy to reduce the frequency, severity, and the duration of the attacks, and thus reducing the risk of medication overuse (26). The FDA has approved

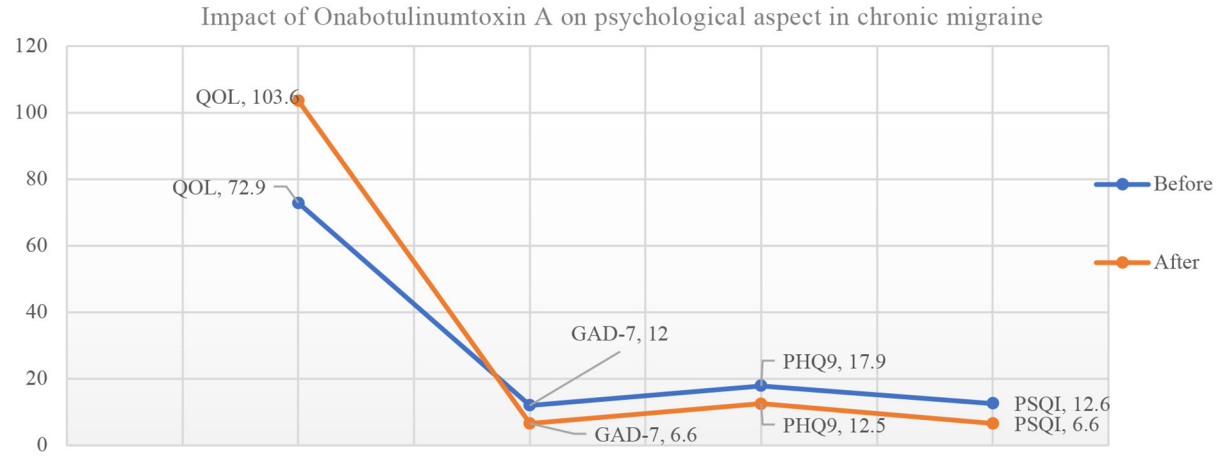

FIGURE 1 | Impact of Onabotulinumtoxin A on psychological aspect in chronic migraine patients ($N = 113$). QOL, Quality of Life; GAD-7, Seven-item Generalized Anxiety Disorder; PHQ9, Patient Health Questionnaire; PSQI, The Pittsburgh Sleep Quality Index.

TABLE 3 | Improvement of psychological aspects and treatment satisfaction with Onabotulinumtoxin A in both genders.

Variables	Males ($N = 15$) *N* (%)	Females ($N = 116$) *N* (%)	*P*-Value
QOL	9 (60)	72 (62.1)	0.877
GAD-7	10 (66.7)	71 (61.2)	0.683
PHQ9	9 (60)	68 (58.6)	0.275
PSQI	11 (73.3)	67 (57.8)	0.869
Treatment satisfaction	7.87 ± 1.96	7.12 ± 2.24	0.221

QOL, Quality of Life; GAD-7, Seven-item Generalized Anxiety Disorder; PHQ9, Patient Health Questionnaire; PSQI, The Pittsburgh Sleep Quality Index.

TABLE 4 | Correlation between disease duration and treatment satisfaction or improvement of psychological aspects.

Variables	Age	Gender	Disease duration	Education	Treatment satisfaction
QOL	$R = 0.007$	$R = 0.014$	$R = 0.003$	$R = 0.142$	$R = 0.294$
	$P < 0.383$	$P < 0.878$	$P < 0.9710$	$P < 0.106$	$P < 0.001$*
GAD-7	$R = 0.005$	$R = -0.036$	$R = -0.006$	$R = 0.172$	$R = 0.239$
	$P < 0.952$	$P < 0.685$	$P < 0.942$	$P < 0.049$*	$P < 0.006$*
PHQ9	$R = 0.066$	$R = -0.014$	$R = 0.42$	$R = 0.79$	$R = 0.195$
	$P < 0.453$	$P < 0.870$	$P < 0.635$	$P < 0.368$	$P < 0.0265$*
PSQI	$R = 0.034$	$R = -0.096$	$R = 0.058$	$R = 0.158$	$R = 0.239$
	$P < 0.699$	$P < 0.277$	$P < 0.508$	$P < 0.071$	$P < 0.006$*

**significant, QOL, Quality of Life; GAD-7, Seven-item Generalized Anxiety Disorder; PHQ9, Patient Health Questionnaire; PSQI, The Pittsburgh Sleep Quality Index.*

of Onabotulinumtoxin A for the prophylactic treatment of chronic migraine in 2010 (10). Its efficacy, safety and tolerability, were proven by the largest migraine therapeutic trial PREEMPT (27).

The analyses conducted in this study concluded that the majority of participants with chronic migraine were aged 45 years old on average, which is consistent with previous studies reporting that people in this age group are most likely to be affected by chronic migraine (28, 29). It was also noted that the majority of the participants were satisfied with their treatment. In addition, the study showed a significant improvement in the quality of life of patients with chronic migraine, which can be attributed to the successful migraine relief. This finding is consistent with previously reported studies (27, 30).

The mechanism by which Onabotulinumtoxin A decreases the burden of the disease is not entirely known, but it is theorized that Onabotulinumtoxin A works on the central, and peripheral sensitization and injecting the trigeminally innervated craniofacial cervical region will blocks the peripheral sensitization by inhibiting the release of pain mediating peptides, specifically CGRP (31).

Also, of note, anxiety and mood disorders have been shown to be closely associated with migraine (32, 33). It is documented that generalized anxiety disorder is 2–10 times more likely to affect migraineurs than the general population (32, 34). These psychiatric comorbidities may influence the prognosis of migraine as they have been associated with a poorer quality of life, increased suicide risk, and they are risk factors for progression of migraine from episodic to chronic (19, 32, 34). These results showed that Onabotulinumtoxin A used for the treatment of migraine helped with depression and anxiety in these patients, as there was a significant improvement in the PHQ-9 and GAD-7 questionnaires for depression and anxiety, respectively. This result was consistent with previous published studies (11, 35) that found that Onabotulinumtoxin A is associated with a reduction in the frequency and impact of migraine

attacks. The studies also concluded that Onabotulinumtoxin A led to an improvement in the symptoms of depression and anxiety, for which the exact mechanism is not entirely clear yet. However, this may be attributed to either the placebo effect on headache and mood disturbances, or it can be due to the reduction of headaches, with a secondary reduction in depression and anxiety (35). On the other hand, there is some evidence that Onabotulinumtoxin A also can help in depression and anxiety independent of its effect on the improvement of migraine (36, 37). Therefore, using Onabotulinumtoxin A in patients with chronic migraine and other psychiatric comorbidities may be an excellent choice. Studies have also noted the cyclical relationship between migraines, stress, and anxiety, which can mean that the use of Onabotulinumtoxin A can lead to a decrease in migraine episodes both directly and indirectly through its effect of reducing anxiety and depression (38).

Moreover, previous Studies have shown a significant association between migraine and sleep disturbances (39, 40), as sleep disruption is common among migraine patients and can even trigger a migraine attack (41). The results of this study showed a significant reduction in the last visit compared to the first in the PSQI, which was employed to measure the quality and patterns of sleep. This is similar to the finding in a previous cross-sectional case control study that found PSQI scores increased with the increase in the frequency of migraine (41).

Satisfaction for treatment which reflects treatment-related migraine improvement correlated significantly with improvement of the investigated psychological aspects.

Some of the participants reported some of the documented side effects resulting from Onabotulinumtoxin A treatment, which included neck pain and stiffness, lateral eyebrow elevation, ptosis, and these adverse events were mild and reversible. These side effects are well-documented in studies that looked to Onabotulinumtoxin A efficacy (28). However, the number of patients experiencing these side effects was minimal 10(8.8%), and these adverse events was mild and reversible and did not impact quality of life in our cohort.

CONCLUSION

This cohort study concluded that Onabotulinumtoxin A improves not only migraine symptoms in chronic migraine patients, but it also leads to significant improvements in psychological aspects in chronic migraine patients, leading to improvements in the quality of life, anxiety symptoms, as well as sleep disturbances. We believe that treating migraine patients should be targeting all these aspects since they are definitely synergistic to each other, they are bidirectional and treating one will improve the other and vice versa. Onabotulinumtoxin A may has the ability to do so without the need to use pharmacological agents.

STRENGTHS

This is the first study to be conducted in Kuwait in order to study the association between Onabotulinumtoxin A use for treatment of chronic migraine and psychological aspects and symptoms in chronic migraine. Another strength is the appropriate sample size and prospective study for 3 years. Nevertheless, some limitations were identified.

LIMITATIONS

The limitations of the study are as follows: (1) the sample was chosen from the patient list in Ibn-Sina hospital, which may not completely represent all chronic migraine patients in Kuwait; (2) in addition, the study researched symptoms of psychiatric illnesses, whereas future studies can be dedicated to studying the effect of Onabotulinumtoxin A on patients with specific diagnoses concluded by psychiatrists through applying Diagnostic and Statistical Manual of Mental Disorders (DSM-5); (3) the study did not include a placebo group; (4) finally, the study did not report on the use of medication prior to initiation of Onabotulinumtoxin A treatment.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the ethical committee of Ibn Sina hospital. The participants provided written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

JA-H designed the study and reviewed the manuscript. HK, OA, FB, SM, and SA performed data collection and drafted the manuscript. DY and RA reviewed the manuscript, performed data collection and drafted the manuscript. SF performed statistical analysis, drafted, criticized, and reviewed the manuscript. All authors read and approved the final manuscript.

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