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EDITORIAL

TEACHING ARTICLE

ORIGINAL ARTICLES

CASE REPORTS

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Editorial

Artificial Intelligence for the Ethiopian Health System: Blessing or curse?

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Though Ethiopia has achieved a lot in reducing morbidity and mortality and increasing life expectancy (1), there are still lots of bottlenecks for the health system. The health system is characterized by limited quality, equity, access to health services, efficiency, adaptive management, resilience and sustainability. Therefore, the country needs innovative, resilient, complexity aware and adaptive health system to meet these challenges and sustain the progress achieved so far.

The global community is already exploring and testing emerging technologies such as Artificial Intelligence (AI) which is among one of the greatest innovations of the 21st century to combat the above-mentioned bottlenecks of health systems. What can AI contribute to the Ethiopian health system? What are the possible opportunities and challenges in order to adapt AI as an innovation to the Ethiopian health system? This editorial tries to give some insights on these issues based on local context and global experience.

Anticipated and preliminary evidences on the benefits of using AI in the healthcare system mainly revolves around improved diagnosis and patient monitoring, medical imaging, assistance in clinical decision making and team work, human resource management, telemedicine, robotic surgery, supply chain management of medical equipment, reduced healthcare cost, research and data analytics (2, 3). AI can be a very good weapon to combat several social determinants of health such as geographical barriers and transport challenges by creating an opportunity to work remotely or mentorship and supervision of healthcare workers. It may also improve patient appointment and adherence by creating cues and reminders for treatment and follow-up. It is also hoped that AI may bring in a dramatic shift from population medicine to personalized healthcare by enhancing precision medical care and decision making.

A recent systematic review has indicated that the main potential challenges in using AI for health system included; 1) patient privacy concerns and ethical considerations in patients personal and sensitive information, 2) poor quality and quantity of data helpful to create algorisms which was the case that during the time of COVID-19 due to lack of quality and adequate data the prediction ability of AI models were limited or not accurate (4), 3) society and patient awareness, and 4) the healthcare workers AI literacy and digital technology maturity (3).

In Ethiopia, though there are good initiatives and intentions in digitalization of healthcare, there are several prerequisite challenges for AI. Still the healthcare system is struggling to transit from manual and paper-based system to digital system. For example, the digital ecosystem such as technology infrastructure including electricity and internet access, human resource capacity, leadership commitment and digital health and data use culture and literacy are lagging. The status quo cognitive bias to unlearn old manual systems can also be bottlenecks on the journey to digitalization and AI adoption in the Ethiopian health system (5). As a result, behavioral resistance and mistrust from the healthcare leadership, healthcare workers and the community when they find the dramatic shift of the humanistic touch healthcare to machine or AI assisted system can be anticipated like as in any other innovation.

The use of AI within the Ethiopian health system is not common except that some anecdotal evidence indicated that students and staff at medical and public health schools have started using AI such as ChatGPT to generate research titles and/or ideas, literature search and searching medical information. The fear here is the academia is not ready in establishing a system to control potential plagiarism, irresponsible use of AI and related concerns in the field. In this regard, the practice of AI within the research community should look ahead of the system to filter and prevent its disadvantages. On the other hand, we do not have evidence on how much AI is practiced among healthcare workers in Ethiopia while most of them have smartphone and may be with ChatGPT within their pocket.

Therefore, in order to benefit from the promised advantages of the emerging technologies of AI and minimize potential harms, the Ethiopian health system should work on improving digital infrastructure, human resource capacity and digital literacy/culture, governance legislation and policy is needed. Anticipating the future and making a good start is wise, easier and cost effective than reversing a spoiled health system.

Finally, whether we like it or not, AI is coming to the healthcare field with a blink of an eye. Whatever it brings as a blessing or a curse or both, the Ethiopian health system needs to complete its own homework to fight and/or adapt or welcome AI before it is too late.

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Teaching Article

Exploring Ethical Research Practices in Ethiopia: Philosophical, Cultural, and Social Reflections – An Educational Perspective

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Abstract

Background: *In the current globalized scientific research environment, effective and responsible research across cultures requires researchers and their institutions to conduct themselves in culturally sensitive ways. The contract between researchers and society involves knowledge of and respect for cultural values and belief systems. It is increasingly recognized that engaging the local community as a partner, rather than imposing demands, helps to build mutually beneficial research cooperation and partnerships. This exploration explains some of the gaps that can be created between the researcher and the researched by cultural, political, socioeconomic, and other differences.*

Methods: *This study reviews literature and considering the following exploratory points. If there is a philosophical, and historical background in Ethiopian society that could be linked with research ethics and communication, and if there are cultural factors in Ethiopia that could influence doing research ethically.*

Conclusion: *To enhance a responsible and balanced approach towards research ethics in Ethiopia, a clear understanding of the social, human, and cultural meaning of informed consent, privacy, and the rights of the individual and the protection of personal, family, or local community interest must be considered. To conduct research responsibly, the involvement of the community, including key decision-makers in healthcare, ethics, research policy, governance, and science is crucial.*

Keywords*: Research ethics; Philosophy; Culture.*

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Introduction

Research plays an essential role but it must be based on sound scientific and ethical principles, including community participation, informed consent, and shared benefits and burdens (1). From a historical perspective, the development of ethical principles for the conduct of health research was influenced by many past atrocities involving the abuse of human beings in medical research (2). These experiences eventually led to the development of ethical codes and regulations: the Nuremberg Code (1949); Declaration of Helsinki (1964-2000); The Belmont Report (1979); CIOMS Guidelines 1982 Rev. 2002; WHO, UNAIDS, TDR Standard Operating procedures; ICH Guidelines for Good Clinical Practice 1990; Good Clinical Practice (1996); UNESCO Universal Declaration on Bioethics and Human Rights 2000(3).

These documents helped raise awareness of ethical challenges in research involving human participants; the rights of research participants the obligations of researchers and the duties of research ethics committees (3,4). The primary goal of health research is the generation of useful knowledge about human health and illness. Ethical requirements are needed to ensure that the rights and welfare of subjects are respected while contributing to the generation of knowledge. Research should avoid causing harm, distress, anxiety, pain, or any other negative feeling to participants. Participants should be fully informed about all relevant aspects of the research before they agree to take part. The challenge for researchers is to take a variety of ethical and practical considerations into account in order to negotiate and find an acceptable balance between general research ethics principles and particular real-world situations. (5, 6). The most powerful and well-resourced research institutions are predominantly in the developed world while the greatest burden of disease is in developing countries. Conducting research in developing world settings tends to be less expensive than in developed ones, and research participants may be easier to recruit for biomedical research where local

healthcare access is limited (7, 8). One prominent problem with the research relationship between developed and developing countries involves ethical double standards: many studies have been done in the Third World that would be considered unethical if conducted in the countries sponsoring the work. For instance, a trial on Mother-to-child HIV transmission conducted by the National Institutes of Health in a number of developing countries used a placebo arm despite the fact that zidovudine had already been clearly shown to cut the rate of vertical transmission greatly and was recommended in the United States for all HIV-infected pregnant women (9, 10). Such conflicts about standards of care in international clinical trials are challenges in global health research (8).

It is clear that health research, no matter where it occurs, needs to be responsive to a number of ethical concerns: having a valuable (and locally relevant) scientific question, using valid scientific methodology, selecting subjects fairly, having a favorable risk-benefit relationship, reviews by an independent committee and voluntary informed consent. How these concerns are understood and met is bound to be influenced significantly by local cultures, religions, and ethnic traditions (11, 12). For instance, some cultures have spiritual or magical beliefs about the origins of disease, and it is sometimes difficult to reconcile these beliefs with the tenets of science and modern medicine (13). Western thinking is strongly characterized by the values of self-reliance, and self-realization. (14, 15). In some cultures, these ways of thinking and their assumptions may be less strongly present and to some extent alien. Research ethics as commonly understood often does not give much argumentative weight to traditional values, but in other settings, collective values and interests may be seen as more valuable than the perspective of individuals; religious norms can be considered indispensable sources of social connection and self-esteem (16).

To conduct research responsibly in Ethiopia, it is important to investigate its history, philosophy, culture, language, customs, expectations, and the aspirations of its ethnically heterogeneous community. There are no publications available to compare the reviews in this context, and given the limitations, this exploration explains some of the gaps that can be created between the researcher and the researched by cultural, political, socioeconomic, and other differences. These gaps if not understood and treated, can hinder the responsible conduct of research. The study concentrates on Ethiopia, where health research is sponsored by foreign and local institutions conducted by both Ethiopians and non-Ethiopians. By identifying some of these gaps, suggestions will be forwarded so that researchers can avoid pitfalls when conducting research with human participants in Ethiopia.

Methods

This study reviews literature and considered the following exploratory inquiries.

1. Is there a philosophical, and historical background in Ethiopian society that could be linked with research ethics and communication?
2. Can the Ethiopian philosophy of 'Yilungnta' influence conducting research ethically in Ethiopia?
3. Are there cultural factors in Ethiopia that could influence doing research ethically?
4. What roles do Ethiopian civil societies, and community leaders/institutions play during research undertaking (participant recruitment, data collection, and dissemination)?
5. Is there a historical and philosophical background in Ethiopian society that could be linked with research ethics and communication?

The emergence of what came to be the nation called Ethiopia can be traced back to a period that begins with the ancient hominoids of Australopithecus and extends to the early inhabitants of the pre-Aksumites (the dominant kingdom at the turn of the first millennia). As confirmed by paleontological data, Homo erectus evolved from Australopithecus afarensis (discovered in 1974) which expanded out of Africa to populate Eurasia 1.8 million years ago (17). The ancient city of Axum became a political, economic, and cultural center in the region. The Axumites dominated the Red Sea trade by the 3rd century. By the 4th century, Axum was one of the few nations in the world, along with Rome, Persia, and Kushan Kingdom in northern India. In 333 A.D, Ethiopian Emperor Ezana adopted Christianity; this was the same year the Roman Emperor, Constantine converted (18). The importance and long history of Ethiopia are reflected in the fact that the word Ethiopia appears in the Bible numerous times (19). The classical language of Ge'ez has a vowel system that has evolved into Amharic, the official language of Ethiopia It is the only indigenous writing system in Africa that is still in use. Many apocryphal texts such as the Book of Enoch, have been preserved in their entirety in this language. Ge'ez is to Ethiopia as Latin is to the west. Ge'ez is the precursor of Ethiopia's Amharic, Tigrinya and Tigre languages (20).

ZeraYacob (1599-1692) wrote 'The Hatata`[that is compared by scholars to Descartes' 'Discourse de la method (1637)] in the Ge'ez language (21). As the historian Sumner writes of his discovery of the Hatata: "It was June 1962. I was then writing the manuscript of the Philosophy of Man, a vast inquiry into the notion of man throughout history, from the Upanishads of ancient India to logical positivism in our days. At that time I was completely ignorant, not only of the content of Ethiopian Philosophy, but even of its very existence … I therefore went to the archives of the National Library. At that time the archives section was poorly lit. The halo of my flashlight was gliding along the shelves when suddenly it quivered on a rather big manuscript covered with wooden boards whose title startled me: "The Book of the Philosophers"! Well then! There was a philosophical manuscript in Ethiopia! It was written in the ancient Semitic language

called Geez which survives only mostly in the liturgy of the church. This is how my adventure started. I was searching for the human, I found the African." (22)

The Ethiopian people are ethnically heterogeneous. Each speaking dialect of one or more languages, At present, around eighty languages are spoken. (23)

From 1529-1632, Ethiopian history was marked by hardships and civil war, where much damage was done to the religious and cultural life of the country. In 1528, the Islamic offensive led by Ahmed Gran caused damage to the cultural inheritance of Ethiopia. However, the heritage of Ethiopian written literature survived, which allowed the people to record their thoughts, philosophy, and traditional wisdom, and transmit it from generation to generation. It was during that time, that ZeraYacob (1599-1692), a 17th century Ethiopian philosopher, was born (24).

In his philosophical investigation, ZeraYakob put man at the center and came up with his ethical principle which was based on man as a preeminent symbol; His message contributes to the betterment of human life (25). Even though written philosophical documents are scarce, the linkage between understanding Ethiopian philosophy and doing research ethically can be assessed.

Fundamental elements in Zara Yacob's philosophy

1. Zara Yacob's Ethiopian Ethical Yelugnta (ይሉኝታ) -Selflessness or Public Self-Consciousness:

Utilitarianism and ethical egoism are goal- and outcome-oriented philosophies. The first aims to make the world a better place for all, and the latter to make the self the beneficiary of one's activities (14). Zara Yacob's ethical 'Yelugnta' has similarities and differences from utilitarian and deontological views.

According to Zara Yacob's ethical Yelugnta, acting ethically means acting according to the perception that others may like the act or that they may feel good about it. By incorporating the perceptions of others into the definition of ethical conduct, an action can be ethically good even if it is 'self-regarding', as long as it accords with what others would also find well (22,25).

Humanity in any culture and society has its own philosophy. Ethiopia has a unique, diverse culture, beliefs, history, and philosophy. Communicating with the Ethiopian community needs a prior understanding of what is inherent in the outlook of the society particularly with the Yilugnta philosophy. For instance, we do not explain or show our sympathy to our loved ones. We simply keep it in our hearts; we cannot impose the food habits of another country only by accepting the nutritional value of some food items (frogs, grasshoppers, dogs, horses, some wild animals, etc.); raw meat consumption is exotic among Ethiopians but could be offensive to other cultures; Eating from the same plate is our food etiquette, etc. Communities have different mindsets and whenever we approach them to do any research the outcome will depend on what the community accepts. Besides ethics as a moral responsibility of all Right or wrong that can have legal implications.

2. Theory of truth, Ayenehelina- (አይነሕሊና) "the light of our will"; Ayenelebona-(አይነልቦና) "light of our hearts". ZeraYakob wrote, "As my faith appears true to me, so does another find his own faith true; but the truth is one." (22). Literally means the mind's eye/Ethiopian third eye. It is a state of philosophical and psychological stability and tranquility, a sense of the truth and a total surrender to it.

3. Zara Yacob's rational inquiry: Hatata (ሐተታ) - meaning 'inquiry`: Everything (including faith) should be subjected to rational inspection before it is accepted. In this regard, Yakob was impartial and anti-traditional, rejecting all prejudices (religious or personal, indigenous or exotic) that did not survive his rational inquiry; this aspect of his thought is close to that of his contemporaries in the European Enlightenment.

ZaraYacob's approach implied a radical understanding of the self as subject and object in relation to problems and their solutions. In order for humans to be self-governing in the realm of moral life, they must at all times consult the Law of God and the Law of humans; it is the Law of God that completes the incomplete and deficient Law of man. He exposed the falsity of blind faith of religious tenets on fasting and celibacy, and marrying more than one wife. Moreover, in his book of 1667, ZeraYacob proclaimed that a man and woman are one in marriage and have equal property rights. Yacob also wrote on women's rights and Human rights in general, criticizing slavery as well as any form of violence against humans (22, 25)

1. Can the Ethiopian philosophy of 'Yelungnta' influence conducting research ethically in Ethiopia?

Ethiopian philosophy (Yilungnta) and research ethics

'Yelungnta' is not just a philosophical concept used exclusively by academics.

culture and makes an impact on everyday life and behavior. As mentioned, Ethical Yelugnta (unlike utilitarianism) does not involve transcending the interests of the self in order to further the greater good of society. Acting well according to Yelugnta is an act that is conducted on the perception that the act is good as seen, and could be regarded as such, by others (25).

Implications of 'Yelugnta' for research ethics

In Ethiopia where the spirit of 'Yelugnta' is prominent, there is a tendency towards a certain conformism. People tend to believe that 'doing the right thing' means pleasing their real peers. In research, this attitude could hinder individual creativity and progress. On the other hand, it could also facilitate the conduct of research involving human participants, in ways that are ethically questionable as religious, civil society leaders and authoritarian rulers may be less threatened guided by Yelugnta.

Researchers may find it relatively easier to select a population and recruit participants for risky health studies. Yelungnta could motivate persons to act in ways that would please those perceived as worthy of respect. Ethiopians feel obliged to do something if asked, believing that refusal would not just be an expression of personal choice, but an ethically wrong thing to do. This obviously relates to the issue of voluntary informed consent for research.

In so far as they follow Yelugnta, do Ethiopias have the ability to refuse participation in a research study when asked to join, or the ability to end participation once they have joined? The same concern can be posed at the community level: when researchers (particularly from respected institutions) approach communities about conducting studies involving their members, will local leaders have a real choice to refuse consent? While this is a concern for all research studies in all regions of the world, in Ethiopia Yelungnta powerfully combines obedience to authority, peer pressure, and moral obligation.

Simply informing participants that they are free to join or refuse to join a study is unlikely to be sufficient. Yelungnta is also reflected in speech and communication: Ethiopians tend to speak in quiet tones, use indirect speech (metaphor and quotation), and make subtle, witty remarks involving implication. With this in mind, insider knowledge of Ethiopian culture is essential in order to conduct the consent process in a way that ultimately conveys the appropriate information, but does not come across as aggressive or confrontational.

Yilugnta has a positive side of respecting others and an interest in listening to others' thoughts, Its negative side is putting aside personal interests, while openness, free thoughts, and individual interests could be jeopardized.

Are there cultural factors in Ethiopia that could influence doing research ethically?

Common customs and research ethics

There are elements of Ethiopian culture important for the responsible conduct of research.

Ethiopian naming customs

Like Western countries, in Ethiopia, there is no family name inherited from generation to generation. Ethiopians are given one name at birth, and the biological father's name is added. In research publications, editors and publishers often confuse Ethiopian names by erroneously looking for a "family name" or surname, which does not exist. For example, if Beyene Wondafrash is cited as Wondafrash B. and if my sister is Beletu Wondafrash that will also be Wondafrash B. It will be difficult to identify who is who in publications. Another example of disfigured name citation is: If Maza Haile-Yesus is cited as Yesus M. simply with the intention of making a family name, Ethiopians will find this amusing because Maza now possesses an Amharic translation meaning Miss Jesus. But Haile-yesus is one 'poly name' (father name in this example) Hence, Ethiopian authors tend to write their full name (given name and father's name and if necessary include grandfather's name to differentiate from another duplicated name) so that authorship problems and confusions can be clear (26)

Besides publication ethics issues, there are other issues regarding names in Ethiopia that can impact the responsible conduct of research. To respectfully address individuals, for instance in official documents, and for some written and verbal communication, individuals are addressed with their cultural honorific title followed by their first name. "Ato" meaning Mr, "Woizero" meaning Mrs., and "Woizrit" meaning Miss, are used to address a man, married woman, and unmarried woman respectively. 'You' as in the English language is not applied across both sexes. 'Ante' for male 'Anchi' for female and 'Eirso" to respect both sexes are used. The relationship between researchers and research participants is based on trust especially when research is conducted by foreign scientists and institutions, it is important that persons are named and addressed with the appropriate terms. For this reason, it is important to confirm the appropriateness of the prefixes used in research information sheets and consent forms. Errors can be insulting and compromise relations during the conduct of research.

Family and kinship relations

In Ethiopia, the extended family remains the focus of the social system. Family needs are put before all other social obligations, including business affairs. For instance, in some parts of Ethiopia, if a family member is killed by someone either by chance or purposefully there exists a so-called "blood feud" culture where the perpetrator is not excused, but instead hunted and killed by male brothers and other male relatives of the victim. The killing of the perpetrator is regarded as a way of honoring the dignity of the victim and the victim's family (31). This aspect of common morality obviously can be a matter of concern if there is a question of research-related harm, in certain communities in Ethiopia. The researchers who conduct

risky research procedures may find themselves at risk for serious harm, and not just legal sanction, though there have been no documented reports yet. Obviously, any health research study that risks causing serious harm is liable to lose community support and future long-term collaboration (30)In this case, researchers in Ethiopia have to be highly vigilant to avoid the risk of harm, potential for harm, and even the appearance of harm.

Social etiquette

The coffee ceremony is considered a central social occasion in Ethiopian life. Coffee is the national drink and its drinking is a ritualized process that generally takes at least an hour or more. The coffee ceremony commonly includes a large group of family members, neighbors, and friends (roughly 5-10 people). Many important issues are discussed at the coffee ceremony, including family, local, and political disputes. Given its social importance, it is considered impolite to refuse an offer to join a coffee ceremony. Historically, coffee has also been a significant agricultural commodity for Ethiopia. The ceremony's significance culturally has evolved over time, however, at its core, it remains a community-building tool, a time to connect with friends and family and to catch up on news and events (32). In research studies, the coffee ceremony can be important to discuss proposed research activities in the community or at sites to conduct research, particularly focus group discussions but people may also talk to others about information shared within the FGD which needs a systematic approach. During meals, participation in conversation is considered polite, and excessive attention to the meal is thought to be impolite. Only the right hand may be used for eating. Ethiopian greetings are intricate, and greetings should never be rushed. People of the same sex may kiss three/four times on their cheeks. Men should wait to see if a woman extends her hand. In the Oromo and southern nationalities they grasp each other's hands and kiss the top of the other person's hands. Elders should be greeted first. It is customary to bend over when introduced to someone who is older or has a more senior position. When an elderly person or guest enters a room, it is customary to bow and then stand until that person is seated (33). Understanding the cultural context could help keep smooth relations with the community. Honor and dignity are crucial to Ethiopians. Disrespect, verbal harassment, dishonesty, and not keeping promises, are all intolerable. For instance, to demonstrate honesty and integrity, orthodox Christians put black thread around their neck to show every kind of truthfulness and obedience to humans and the almighty. In traditional Christian Ethiopia, there are around 250 days of fasting per year. During fasting days it is prohibited to consume animal products. Researchers therefore need to respect the customs and symbols of the society, when approaching potential research subjects and initiating study activities.

Ethiopia is nicknamed "the land of 13 months of sunshine". The New Year starts in September and each month has 30 days. The Ethiopian calendar also has an extra five-day month called Pagume (ጳጉሜ). Each month has a meaning related to seasonal changes and the life of the community. Day and night contain 12 hrs each, and there is no 24 hrs. system. There is also an eight-year gap between the Ethiopian and Gregorian calendars.

Official calendars are published incorporating both local and Gregorian systems. Without adapting to this calendar system, researchers may create confusion when they develop a work plan for research, conduct formal communications, and set appointments. Even though the calendar may create problems during the research process when one is not accustomed to it, this does not create a practical problem for the nation. It is rather part of what makes Ethiopia unique and ties its present day to the past (28).

What roles do Ethiopian civil societies, and community leaders/institutions play during research undertaking (participant recruitment, data collection, and dissemination)?

Ethiopian civil societies and social welfare for researchers to consider

There are many different types of Ethiopian social institutions, locally grown means of managing lives. The most prevalent are Eidir (burial services and condolences), Debo (temporary labor unions), Eikub (saving unions), Mahiber (social group), Shimglina (mediation), Afersata/ Awchahne (community consultative resolution), Shengo (advisory team), Gadaa system (expression of Oromo civilization.) etc. (27)

Civil society's custom/culture in Ethiopia: some definitions and examples

Afersata or Awchahne: a social system that treats all 'civil or criminal cases' in traditional ways. If research is conducted in a community with such a system, legal concerns about the research (such as conflicts of interest) should normally engage with these local ways of resolving disagreements. To do otherwise may bring further complications.

Gada system: the Oromo democratic political and social institution that governs the life of individuals in the society from birth to death advocating the belief that all people should have equal political, social, and economic rights.

Debo: a labor exchange group whereby groups work together to complete certain communal projects on time, such as building construction, weeding, and harvesting.

'Equb': a local social support system used to assist those with financial and other needs. Local communities pool money and each month someone will take the collected money to use for his/her own purposes. Since this is a kind of collective association, the power of the social support system extends beyond finance; sometimes Equb may be helpful for conducting research in the

community or to consent individuals within the association.

Idir: a burial association for mutual support in relation to funerals. Considered as a third party between governments and family.

Shimglina/MehalSefari: 'The one that camps at the center.' Refers to those community leaders who take centrist or neutral positions on fairness and social justice, and advocate for a peaceful and fair resolution of any conflict. This can be useful in resolving research-related conflicts. In some societies, health is viewed from a religious and taboo angle which is sometimes difficult to reconcile with modern medicine. Notions like Evil eyes, witchery, and fortune-telling influence health behaviors. These customs can affect the implementation of health intervention strategies.

Invasions of privacy, breaches of confidentiality, stigma, and rejection by families or Communities, and social harms could happen if we do not take into consideration the influence and the roles of civil society institutions and stakeholders in the Ethiopian context. A country`s identity has influences on basic human values, priorities, beliefs, and behaviors. Understanding and respect for Ethiopia's history, philosophy, culture, traditions, and customs through acknowledgment of its community values, differing worldviews, and moral practices are essential for the responsible conduct of research in this country (27, 29).

As we live in a time of scientific and technological advancement, moral and philosophical preconceptions about the world in which we live are challenged by new discoveries and innovations. To achieve a credible balance between the progress of science and the protection of the rights of individuals and their cultural values, researchers require ethical norms which are acceptable internationally but which are sensitive to cultural diversity. We must also adapt our traditional concepts in the face of changes in a context of interaction and interdependence on an international scale. On the other hand, existing ethical codes may not always sufficiently address the issues of multiple and complex cultural and contextual differences.

In Ethiopia, higher education institutions, particularly Jimma University, implement translational community-engaged research guided by the motto: 'We are In the Community'. In this regard, to do research ethically means taking into account cultural and contextual differences among researchers, among participants, and between researchers and participants (34).

Ethical principles can be truly respected through practices based on local values, collaboration, consensus, communication, negotiation, and partnerships. Research design, informed consent, participant roles, entry into the field, approaches to data collection, and dissemination of results must be contextualized by respecting local tradition and cultural values integrated into the process through dialogue and not by imposition. Cultural differences must be evaluated carefully to undertake research for better outcomes and prevent misunderstandings, stereotyping, cultural barriers, or interpersonal conflict before, during, and after data collection.

Conclusion

To enhance a responsible and balanced approach towards research ethics in Ethiopia, a clear understanding of the social, human, and cultural meaning of informed consent, privacy, and the rights of the individual and the protection of personal, family, or local community interest must be considered. To conduct research responsibly, the involvement of the community, including key decision-makers in healthcare, ethics, research policy, governance, and science is crucial.

Research should adhere to the highest international standards and ensure that there is no danger of exploitation of the participants of vulnerable populations. This could be achieved through capacity-building exercises, and collaborative networks by understanding the challenges and opportunities of modern science and technology advancement. To do research ethically, through the ethics of beneficence and maleficence, understanding ethical dilemmas and Decision making, promoting the National Research Ethics Review System, Strengthening ethical review capacity within countries by considering the complexity of cultural variations, national laws, local medical and research practices, and local knowledge is crucial.

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Original Article

Pattern of Diabetic Retinopathy in a Referral Hospital in Resource Limited setting; Institution Based Cross-sectional Study

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Abstract

Background: *Diabetes mellitus comprises a group of metabolic disorders that share the common feature of hyperglycemia. One-third of the global population of individuals with diabetes is estimated to have diabetic retinopathy.*

Method*: The institution based cross sectional study was conducted at Menilik II Hospital from March 2022 to September 2022 GC. A complete eye exam was performed to reach a diagnosis by a retina specialist using a slit lamp microscope coupled with a 90D lens. Data were entered and analyzed using the Statistical Package for Social Science.*

Results*: In this study, a total of 222 diabetic patients were enrolled. There were 116 males (52.3%). Diabetic retinopathy was mild in 28 (12.6%), moderate in 58 (26.1%), severe in 23 (10.4%) and proliferative in 60 (27%) patients. Moderate and severe visual impairment was observed in 26 (15.1%) patients; 24 (14.2%) had mild visual impairment, and 53 (31.4%) patients were blind. Among the 163 diabetic retinopathy patients who had fasting blood sugar tests, 109 (66.9%) had poor glycemic control. Among the 56 diabetic retinopathy patients who had Hb A1c measurements, 89.5% had poor glycemic control.*

Conclusion*: Visual-threatening diabetic retinopathy is more common in patients with poorly controlled diabetes and requires multi-sectoral collaboration to decrease visual loss*

Keywords: *Diabetic retinopathy, Diabetic macular edema*
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Introduction

Diabetes mellitus comprises a group of metabolic disorders that share the common feature of hyperglycemia. Diabetes is currently classified as type 1 DM or type 2 DM based on the pathogenic process that leads to hyperglycemia (1).

Diabetes is found in every population in the world and in all regions, including rural parts of low- and middle -income countries. The number of people with diabetes is steadily increasing, with the World Health Organization estimating that there were 422 million adults with diabetes worldwide in 2014 (29). In addition, the International Diabetes Federation estimates that 1.1 million children and adolescents aged 14–19 years have type 1 diabetes. Without interventions to halt the increase in diabetes incidence, there will be at least 629 million people living with diabetes by 2045 (2). Ethiopia is one of the five countries with the greatest number of people affected by diabetes in sub-Saharan Africa (3). Diabetic retinopathy is a leading cause of vision loss worldwide among patients aged 25 –74 years, especially in developed countries such as the United States. From 1990–2010, diabetic retinopathy was the fifth most common cause of preventable blindness and moderate to severe visual impairment (4) . One-third of the global population of individuals with diabetes are estimated to have diabetic retinopathy; of that group, one-third are likely to have vision-threatening diabetic retinopathy.

The best predictor of diabetic retinopathy is the duration of the disease; thus, with increasing life expectancy, diabetic retinopathy and subsequent blindness tend to increase. (5,6)

The identification and optimum control of coexisting health and medical problems are critically important because they present a significant risk for the development and progression of diabetic retinopathy. These factors include chronic hyperglycemia, (7,8,9) hypertension, (11,12) renal disease, (1,10) abdominal obesity, hypercholesterolemia, dyslipidemia, cardiovascular

and peripheral autonomic neuropathies. A better understanding of the pattern of diabetic retinopathy can contribute to evidence-based and improved care for patients with diabetic retinopathy.

Methods and Patients

The study was conducted at Menilik II Comprehensive Specialized Referral Hospital from March 2022 to September 2022. The ophthalmology department has general outpatient clinics and five specialty clinics. Each day, 60 to 100 referred new patients seek service in addition to the patients being followed up in various clinics. The retina clinic, a specialty clinic, provides care for approximately 50 patients per day. An institution-based cross-sectional study was used to study the pattern and characteristics of diabetic retinopathy in diabetic patients evaluated at the retinal clinic. All patients above the age of 18 were included except those with opaque ocular media that did not allow adequate visualization of the fundus and retinopathy other than diabetic retinopathy. A total of 222 diabetic patients who received care and follow-up at the retina clinic during the study period and fulfilled the eligibility criteria were included in the study. Informed written consent was obtained.

A structured questionnaire was used to collect the demographic, clinical, and medical history and other characteristics of the study participants. Blood pressure was measured by a manual sphygmomanometer. If the blood pressure was elevated, two blood pressure measurements were taken at five-minute intervals, and the average of the measurements was calculated. Body mass index (BMI) was calculated using the formula (weight in kilograms/height in meters squared) after the weight in kg and height in meters were measured. The vision was determined using Snellen's chart at 6 meters by a trained nurse's right eye followed by the left eye by occluding one eye at a time. The best visual acuity was determined by an optometrist. Visual impairment was classified according to the WHO visual impairment classification. Intraocular pressure was measured using an air puff tonometer before the pupils were dilated. A slit lamp examination was performed to examine the anterior segment of the eye. The pupils were dilated using tropicamide 1%, and the posterior segment was examined using a 90-diopter lens coupled with a slit lamp biomicroscope. Retinopathy was diagnosed and graded by a vitreoretinal surgeon using the ICDRDSS (27). For patients with bilateral DR, data from the most severe eye were selected for analysis. A pertinent laboratory investigation was sent, and the findings were explained to the patient and managed accordingly. In this study, Diabetes mellitus was defined disorder of carbohydrate metabolism characterized by impaired ability of the body to maintain blood glucose level there by as a Fasting blood glucose concentration >126 mg/dl or Random blood sugar > 200 mg/dl, hemoglobin A1c 6.5% or higher or patients taking medication for diabetes. Non Proliferative Diabetic Retinopathy (NPDR) is defined as when there is no new vessels or no extraretinal fibrovascular tissue, while Proliferative Diabetic Retinopathy (PDR) defined when there is new vessels in either iris, optic disc or retina.

Using International Clinical Diabetic Retinopathy Disease Severity Scale (ICDRDSS), No retinopathy; no abnormalities, Mild NPDR, microaneurysms only. Moderate NPDR- more than microaneurysms only but less than severe NPDR; Severe NPDR- any of the following: >20 intraretinal hemorrhages in each of four quadrants, definite venous beading in two or more quadrants, prominent IRMA in one or more quadrants and no PDR; and Very severe NPDR- any patient with two or more of the characteristics of severe NPDR. PDR - retinal neovascularization, vitreous hemorrhage, or preretinal hemorrhage.

As there was no OCT in Menilik II Hospital, ETDRS definitions of clinically significant macular edema (CSME) were used for retinal thickening at or within 500 μm of the center of the fovea, hard exudates at or within 500 microns of the center of the fovea with adjacent area of retinal thickening, and retinal thickening of at least 1 disc area, any portion of which was within 1500 μm (approximately 1 disc diameter) from the center of the fovea. Hypertension was defined as a blood pressure greater than or equal to 130/80 mm Hg, and hyperlipidemia was defined as a serum cholesterol concentration greater than 200 mg/dl.

The International Classification of Diseases II definitions of visual impairment were used: mild visual acuity worse than 6/12 to 6/18, moderate visual acuity worse than 6/18 to 6/60, severe visual acuity worse than 6/60 to 3/60, and blindness defined as visual acuity worse than 3/60. A smoker is someone who smokes any tobacco product, either daily or occasionally. Moderate activity is defined as at least 150-300 minutes of walking at a moderate or brisk pace, and vigorous activity is defined as at least 75–150 minutes of heavy exercise three times a week.

The data were entered into and analyzed using the Statistical Package for Social Science (SPSS) version 26.

The frequency distribution, mean (±SD), range, and ratio were used to summarize data on independent variables. A bivariate logistic regression was performed for every explanatory variable, a p-value less than 0.25 was included in the multinomial logistic regression model, and a p-value less than 0.05 was considered to indicate statistical significance.

Ethical consideration

The research and publication committee of the Ophthalmology department of Addis Ababa University has approved this study to be conducted on 03/02/2022 with letter reference number OREC/002/22.

Results

In this study, a total of 222 diabetic patients were enrolled. There were 116 males (52.3%). The mean age was 56.1 years (SD = 12.116; range: 23–89 years). Oth-

Table 1. Sociodemographic characteristics of diabetic retinopathy patients . March 2022-September 2022 (n=222)

Socio-demographic characteristics	Category	Number	Frequency
Gender	Male	116	52.3%
	Female	106	47.7%
Age in years	20-30	8	3.6%
	30-40	23	10.4%
	40-50	47	21.2%
	50-60	76	34.2%
	>60	68	30.6%
Place of residence	Urban	180	81.1%
	Rural	42	18.9%
Marital status	Single	18	8.1%
	Married	141	63.5%
	Widowed	48	21.6%
	Divorced	15	6.8%
Education level	Can't read and write	18	8.1%
	Read and write	12	5.4%
	Primary school	65	29.3%
	Secondary school	47	21.2%
	Certificate/diploma/degree	80	36%
Occupation	Unemployed	57	25.7%
	Government worker	56	25.2%
	Private worker	58	26.1%
	Retired	51	23%
Average income	<1000	59	26.6%
	1000-2000	58	26.1%
	2000-3000	25	11.3%
	3000-6000	52	23.4%
	>6000	28	12.6%

The mean duration of diabetes since diagnosis was 14.5 years. The majority of the patients (92, 41.4%) had diabetes for at least 15 years. In terms of diabetes treatment, 102 patients (45.9%) were taking oral glucose-lowering agents.92 patients (41.4%) were using insulin, 22 patients (9.9%) were taking oral glucose lowering medications along with insulin injections, and 6 patients (2.7%) were using only dietary management. Hypertension was present in 133 (59.9%), dyslipidemia in 75 (33.8%), neuropathy in 27 (12.2%), nephropathy in 6 (2.7%), heart disease in 12 (5.4%), and stroke in 2 (0.9%) of the patients. Additionally, 12 individuals had a history of smoking, 4 of whom were former smokers. Out of 222 patients, 89 (40.1%) patients had regular and recommended physical activity. Most of the patients (154, 69.4%) were not having eye compliant, and 60 (27%) of the patients had a history of visual reduction. Seventy-one (32%) patients had a history of other ocular illnesses (Table 2).

Moderate and severe visual impairment was observed in 26 (15.1%) patients; and 53 (31.4%) patients were blind. DME was the underlying cause in 25 (19.3%) of the patients with visual impairment. (Table 3). Diabetes retinopathy was severe in 23 (10.4%) and proliferative in 60 (27%) patients. (Table-4). A total of 50 (22.5%) patients had a history of ocular surgery, the majority of whom had cataract surgery (41, 18.5%), followed by glaucoma (4, 1.8%), pars plana vitrectomy (2, 0.9%), scleral buckle (1, 0.5%), and pterygium excision (1, 0.5%).

Table 2 Ocular comorbidities in diabetic patients from March 2022-September 2022 (n=222)

Other ocular illness	Number	Frequency
Cataract	38	17.1%
Glaucoma	12	5.4%
AMD	5	2.3%
Uveitis	4	1.8%
Macular hole	3	1.4%
Retinal vein occlusion	3	1.4%
Corneal opacity	3	1.4%
Hypertensive retinopathy	1	0.5%
Endophthalmitis	1	0.5%
VKC	1	0.5%
Total	71	32%

Table 3: Visual impairment grading in diabetic retinopathy and DME patients in the worst eye from March 2022 to September 2022 (n=222)

Visual impairment in diabetic retinopathy patients	Diabetic retinopathy (Number)	Frequency	DME (Number)	Frequency
Mild visual impairment	24	14.2%	6	20.7%
Moderate visual impairment	26	15.4%	6	20.7%
Sever visual impairment	26	15.4%	5	17.2%
Blindness	53	31.4%	8	27.6%
Total	129	76.4%	25	86.2%

Intraocular injection and laser treatment were given to 41 (18.5%) and 22 (9.9%) patients respectively. PDR patients received the majority of the laser treatments (21 [9.5%]). Two Pars Plana Vitrectomy procedures were performed for PDR patients. Based on clinical examination, Diabetic Macular Edema was found in 29 (13.1%) of patients; only 5 patients underwent OCT examination, and 13 (44.8%) of the DME-diagnosed patients had a history of intraocular injection. High blood pressure was detected in 75 (44.4%) diabetic retinopathy patients. In addition, 98 (58%) of the patients had a normal BMI, and 14 (8.3%) were obese. Among the 163 diabetic retinopathy patients who had fasting blood sugar tests, 109 (66.9%) had poor glycemic control; however, among the 56 diabetic retinopathy patients who had Hb A1c measurements, 89.5% had poor glycemic control. Total cholesterol, triglycerides, HDL, and creatinine were measured for some patients, and high values of each were found in 8 (17.8%) of the 45 patients, 9 (22%) of the 41 patients, 29 (65.9%) of the 44 patients, and 14 (29.8%) of the 47 patients, respectively. Most laboratory investigations and Optical Coherence Tomography were not performed in the hospital, as a result 60.8% of patients did not receive an investigation, and 37.4% of those patients could not afford the tests.

Table 4: Diabetic retinopathy grading in the worst eye between March 2022 and September 2022 (n=222)

Diabetic retinopathy	Male	Female	Total
Mild NPDR	13(5.9%)	15(6.8%)	28 (12.6%)
Moderate NPDR	33(14.9%)	25(11.3%)	58 (26.1%)
Severe NPDR	16(7.2%)	7(3.2%)	23 (10.4%)

Age, duration of diabetes mellitus, sex, dyslipidemia, FBS, blood pressure, and creatinine level were associated with the degree of diabetic retinopathy (p value<0.25), and type of diabetes mellitus, duration of diabetes mellitus, history of neuropathy, and type of diabetes medication were associated with vision-threatening diabetic retinopathy (p value <0.25). Patients who had diabetes for 5 years or 5-10 years had a 17- or 50-fold increased risk of developing diabetic retinopathy, respectively. (AOR = 17.5; 95% CI: 1.13-269.4; and AOR = 49.9; 1.85-1343.3) (Table 5 and 6)

Table 5: Bivariate and multinomial logistic regression analyses of factors associated with diabetic retinopathy between March 2022 and September 2022 (n=222)

Variable			COR	P value	AOR	P value
	Yes	No	(95% CI)		(95%CI)	
Age						
20-30	4	4	0.308(0.069-1.372)	0.12	0	0.99
31-40	16	7	0.703(0.246-2.01)	0.51	0.892(0.27-28.9)	0.94
41-50	38	9	1.299(0.519-3.252)	0.58	0.13(0.005-3.958)	0.24
51-60	59	17	1.068(0.491-2.325)	0.87	0.665(0.58-7.59)	0.74
>60	52	16	1		1	
Sex						
Male	96	20	2.17(1.152-4.088)	0.017	1.22(0.195-7.68)	0.83
Female	73	33	1		1	
Type of diabetes						
Type I	34	10	1.083(0.494-2.372)	0.842		
Type II	135	43	1		1	
Duration of diabetes						
<5years	27	17	0.36(0.16-0.8)	0.013	17.5(1.13-269.4)	0.04
5-10years	29	15	0.43(0.19-0.99)	0.048	49.9(1.85-1343.3)	0.02
11-15years	38	4	2.15(0.67-6.84)	0.194	1.36(0.8-22.36)	0.826
>15years	75	17	1		1	
Type of diabetes medication						
Dietary management	5	1	1.47(0.14-15.67)	0.749		
Oral hypoglycemic agent	72	30	0.71(0.24-2.01)	0.529		
Insulin	75	17	1.29(0.42-4.01)	0.651		
Both oral hypoglycemic agent and insulin	17	5	1			
History of hypertension						
Yes	103	30	0.836(0.45-1.56)	0.57		
No	66	23	1			
History of dyslipidemia						
Yes	53	22	1.55(0.82-2.93)	0.18	0.74(0.12-4.52)	0.74
No	116	31	1		1	

History of neuropathy						
Yes	21	6	0.83(0.343-2.36)	0.83		
No	148	47	1			
Adequate physical activity						
Yes	62	27	1.79(0.96-3.34)	0.66		
No	107	26	1			
Blood pressure						
Normal	75	18	0.645(0.33-1.22)	0.182	0.59(0.76-4.68)	0.62
High	94	35			1	
Body mass index			0	0.99		
FBS	163	48				
<126 mg/dl	78		0.495(0.258-0.952)	0.035	15.7(1.8-135.9)	0.12
>= 126 mg/dl	133		1		1	
HbA1C						
<6.5%	6	3	0.667(0.15-2.96)	0.594		
>=6.5%	51	17	1			
Total cholesterol	45	15				
<=200 mg/dl	37	13	0.712(0.133-3.793)	0.690		
>200 mg/dl	8	2	1			
Triglyceride						
<=180 mg/dl	32	12	0.889(0.21-3.85)	0.875		
>180 mg/dl	9	3	1			
High density lipoprotein						
>=30 mg/dl	15	6	0.69(0.2-2.356)	0.55		
<30 mg/dl	29	8	1			
Creatinine						
0.6-1.3 mg/dl	33	15	0.314(0.63-1.56)	0.157	3.053(0.4-23.06)	0.27
>1.3md/dl	14	2	1		1	

Table 6: Bivariate and multinomial logistic regression analyses of factors associated with vision-threatening diabetic retinopathy March 2022-September 2022 (n=222)

Variable	**VTDR**		**COR**	**P value**	**AOR**	**P value**
	Yes	No	(95% CI)		(95%CI)	
Age						
20-30	1	3	0.33(0.33-3.42)	0.35		
31-40	7	9	0.78(0.25-2.4)	0.66		
41-50	21	17	1.23(0.53-2.86)	0.62		
51-60	28	31	0.9(0.43-1.91)	0.79		
>60	26	26	1			
Sex						
Male	50	45	1.318(0.72-2.43)	0.376		
Female	33	40	1			
Type of diabetes						
Type I	20	14	1.63(0.76-3.49)	0.207	0.73(0.29-1.78)	0.49
Type II	63	72	1		1	

Duration of diabetes						
<5years	11	16	0.484(0.198-1.185)	0.112	1.52(0.59-3.95)	0.38
5-10years	11	18	0.431(0.179-1.038)	0.06	2.15(0.87-5.32)	0.95
11-15years	17	21	0.57(0.26-1.25)	0.162	1.64(0.72-3.73)	0.23
>15years	44	31	1		1	
Type of diabetes medication						
Dietary management	2	3	0.278(0.35-2.204)	0.225	4.23(0.48-37.3)	0.19
Oral hypoglycemic agent	29	43	0.281(0.89-0.883)	0.03	3.21(0.98-10.49)	0.53
Insulin	40	35	0.476(0.153-1.485)	0.201	2.28(0.69-7.5)	0.17
Both oral hypoglycemic agent and insulin	12	5	1		1	
History of hypertension						
Yes	54	49	0.711(0.38-1.324)	0.282		
No	29	37				
History of dyslipidemia						
Yes	23	30	1.39(0.72-2.68)	0.316		
No	60	56				
History of neuropathy						
Yes	13	8	0.552(0.216-1.41)	0.215	1.63(0.61-4.37)	0.325
No	70	78	1		1	
Adequate physical activity						
Yes	29	33	1.159(0.62-2.169)	0.644		
No	54	53				
Blood pressure						
Normal	51	43	0.74(0.4-1.36)	0.38		
High	35	40	1			
Body mass index						
FBS						
<126 mg/dl	28	26	1.18(0.62-2.27)	0.62		
>= 126 mg/dl	52	57	1			
HbA1C						
<6.5%	0	6	0	0.99		
>=6.5%	21	30	1			
Total cholesterol						
<=200 mg/dl	12	25	1.44(0.25-8.22)	0.68		
>200 mg/dl	2	6	1			
Triglyceride						
<=180 mg/dl	8	24	1.17(0.2-6.805)	0.86		
>180 mg/dl	2	7				
High density lipoprotein						
>=30 mg/dl	3	12	0.56(0.13-2.47)	0.44		
<30 mg/dl	9	20	1			
Creatinine						
0.6-1.3 mg/dl	11	22	0.9(0.24-3.34)	0.87		
>1.3md/dl	5	9	1			

Discussion

The prevalence of diabetic retinopathy in our study was 76.1%, which is higher than that reported in studies performed in Gonder (16.2%) (24), Addis Ababa (21.6%) (23), and Iraq (33.2%) (28), possibly because the study was performed in a retina clinic where patients are referred for retina examination and additionally studies in Gondar and Addis Ababa dealt only on type II diabetes unlike our study which dealt on both types of diabetes. Of all patients,81.1% of patients had a history of previous diabetic retinopathy screening which will be crucial in early detection of diabetic retinopathy. The most common comorbid condition with diabetes was hypertension in 59.9% of our study participants that comparable with study done in Iraq(44%), Nigeria (69.6%) and Gondar (50.2%). (17, 18, 24). Most of our patients had PDR (27%) and moderate NPDR (26.1%) in the worst eye. This finding is relatively higher compared to studies from Nigeria (3.7%) and Addis Abeba (16.7%). (18,23). This might be explained by the Addis Ababa study focused more on selected type II diabetes patient and the study from kano Nigeria was much lower than from our study and might be due to economic and awareness difference between the two study population.

PDR is also common among smokers despite the relatively low number of smokers. In this study, 40.1% of the participants were adhered to regular exercise which is lower than the study done in Jimma which showed 55.5% of the participant were adhere to regular exercise. (22)

Blindness in the worst eye occurred in 31.4% of diabetic retinopathy patients, which is greater than in studies performed in Gondar (15.2%) and Nigeria (6%). (18,24) .This might be explained by most patients with vision threatening diabetic retinopathy (VTDR) referred to Menelik Hospital from all over the country for final intervention. Other causes of visual impairment other than diabetic retinopathy were found and the most common of which was cataracts. Additionally, cataract surgery was performed on 18.5% of patients. Similar to studies done in Iraq, Nigeria, Gondar and Camerron; patients with duration of diabetes greater than ten years are at greater risk for developing DR (17,18,24,28).

Conclusion

The prevalence of diabetic retinopathy and VTDR at Menelik II Referral Hospital was high. A duration of diabetes of 10 years was associated with the presence of diabetic retinopathy. More than half of diabetic patients have poor glycemic control, and additional risk factors that contribute to diabetic retinopathy development and progression are common.

Therefore, we can conclude from this study that diabetic retinopathy is a visually threatening eye condition that needs due attention.

Limitation of study

The study was done for a short period and will give a narrow spectrum of the problem. There was no OCT machine in the hospital and it was difficult to diagnose macular edema objectively as a result we used clinical examination to diagnose diabetic macular edema.

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Consent to Publication

There was no confidential data or photo of the participant, only informed consent was addressed.

Authors contribution

Dr. Feven Feleke was a principal investigator who collected and analyzed data and Dr. Dereje Negussie was co-investigator.

Conflict of interest

There was no conflict of interest while conducting this study.

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Data availability

Data will be made available upon reasonable request

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Original Article

Profile of Secondary Glaucoma in a Resource-Limited Setup: Institution-Based Cross-Sectional Study

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Abstract

Background: *Prevalence and types of secondary glaucoma varies between countries. This study aims to determine the current clinical profile, proportion, and causes of various types of secondary glaucoma in newly diagnosed glaucoma patients at Menelik II Specialized Hospital.*

Methods: *This hospital-based cross-sectional descriptive study was conducted at a glaucoma clinic between May 1 and July 31, 2022. All newly diagnosed secondary glaucoma patients aged 18 years and above were included. A structured questionnaire comprising socio-demographic data, history, visual acuity, intraocular pressure, slit-lamp, gonioscopy, fundus examination findings, and finally, the diagnosis was used. Data management and analysis were done using SPSS version 26.*

Results: *Four hundred forty-nine newly diagnosed glaucoma patients visited the clinic during the study period. One hundred seventy-three (38.53%) patients were diagnosed to have secondary glaucoma. The leading causes of secondary glaucoma were found to be Pseudoexfoliative glaucoma (75.5%), followed by neovascular glaucoma (7%), uveitic glaucoma (6.7%), lens-induced glaucoma (5%), and miscellaneous causes (5.7%). Secondary glaucoma was a significant cause of visual morbidity, with 57.04% of eyes presenting with best corrected visual acuity of < 6/60, intraocular pressure > 30 mmHg in 45.3% of eyes, and 61.74% with a cup-to-disc ratio of ≥0.7.*

Conclusion: *The leading causes of secondary glaucoma were found to be Pseudoexfoliative glaucoma (75.5%), followed by neovascular glaucoma (7%), uveitic glaucoma (6.7%), lens-induced glaucoma (5%), and miscellaneous causes (5.7%). Secondary glaucoma is a significant cause of visual morbidity. Timely diagnosis and early and appropriate management are essential to prevent irreversible visual loss.*

Keywords: Blindness, Clinical profile, Glaucoma, Neovascular glaucoma, Pseudoexfoliative glaucoma
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Introduction

Glaucoma is a group of disorders with a common denominator of characteristic optic neuropathy, characteristic visual field loss, and often, but not invariably, increased intraocular pressure. It poses a significant public health concern as it is the second leading cause of blindness and a leading cause of irreversible blindness worldwide (1). In the last decades, the prevalence of glaucoma has been increasing rapidly worldwide in line with population growth and ageing. In 2013, the number of people (aged 40–80 years) with glaucoma worldwide was estimated to be 64.3 million, increasing to 76.0 million in 2020. The number of people with glaucoma worldwide will rise to 111.8 million in 2040, disproportionally affecting people residing in Asia and Africa (2). Secondary glaucoma forms a heterogeneous glaucoma group characterized by identifiable underlying secondary ocular or systemic causes, leading to elevated IOP and, subsequently, to glaucomatous optic neuropathy. Etiologies of secondary glaucoma include lens pathology, trauma, neovascularization, steroid use, uveitis, ocular surgery, pseudoexfoliative material (PXF), and any other abnormal ocular and systemic pathologies. The prevalence of secondary glaucoma

varies from 6 to 22% among various studies with varied etiologies(3–7). Despite its public health significance, limited data on secondary glaucoma prevalence, clinical profile, and possible risk factors are available. With improved surgical practices, increased awareness of more people availing to seek ophthalmic services, and increased life expectancy, there is a change in the profile of secondary glaucoma (8). Currently, there is a lack of data on the profile of secondary glaucoma in Ethiopia. This study evaluated the proportion, etiologies, and characteristics of newly diagnosed patients with secondary glaucoma presenting to a tertiary eye care hospital in Addis Ababa.

Methods and Patients

Study design and study population

This hospital-based, cross-sectional descriptive study was conducted among newly diagnosed secondary glaucoma patients at a glaucoma clinic in Menelik II Specialized Hospital, Addis Ababa, Ethiopia, between May 1- July 31, 2022. All consecutive new patients who were 18 years old and above, with a diagnosis of secondary glaucoma, were included. The ophthalmology residents did an ophthalmic examination of patients, and glaucoma consultants confirmed the final diagnosis of all included in the study. Enrolled patients who fulfilled the inclusion criteria were selected and assessed with a structured questionnaire. A detailed clinical history and ocular examination were made. The principal investigator completed the sections on socio-demographic data, presenting complaints, associated symptoms, risk factors, ophthalmic examination, and relevant investigations.

Data collection

The vision was taken using the Snellen chart at 6 meters in both eyes, occluding one at a time. In those who didn't see with the Snellen chart, it was taken by counting the finger (CF) based on the distance the patient could see in a meter. Hand motion was recorded when vision was less than counting the fingers in front. Light perception (LP) with or without projection was recorded when it was less than hand motion. Intraocular pressure (IOP) was measured with I–care in both eyes before dilation and a gonioscopy. Anterior segment findings like corneal oedema, opacity, surgical marks, keratic precipitates, anterior chamber reaction, anterior and posterior synechiae, iris neovascularization, presence and site of PXF, lens pathology, and other relevant findings were noted. A gonioscopic examination was done to determine the status of the angle of each eye using a Sussman gonioscopy lens. A dilated fundus examination was done thirty minutes after applying 1% Tropicamide in both eyes. Both eyes were examined with a slit lamp and a +90-diopter lens. The extent of glaucomatous disc damage on fundoscopy was assessed by evaluating the vertical cup/disc from 11 to 1 o'clock superiorly and from 5 to 7 o'clock inferiorly. Retinal and other optic disc changes were recorded whenever possible.

Operational Definition

Secondary glaucoma was diagnosed when the following criteria were met. Documented history and findings include trauma, neovascularization, steroid use, uveitis, PXF (pseudoexfoliation syndrome), and previous intraocular surgeries. Those surgeries include complicated cataract surgery, vitreoretinal surgery, keratoplasty, or any other abnormal ocular or systemic findings that could have caused IOP elevation with associated glaucomatous optic neuropathy.

Visual field (VF) abnormality was not considered a criterion for diagnosing glaucoma. The other eye was thoroughly evaluated to rule out primary glaucoma. If the optic disc could not be examined because of media opacity (hence, VF test was not possible), then a visual acuity ≤3/60 and IOP exceeding the 99.5th percentile (> 26 mmHg) was taken as sufficient for a diagnosis of glaucoma (9). Secondary open-angle glaucoma is a diverse group of diseases diagnosed when the anterior chamber angle is open on gonioscopy based on the Shaffer gonioscopic grading system and if there is an identifiable cause. An identifiable pathologic cause closes the angle directly or by angle factors such as peripheral anterior synechiae or irido-trabecular apposition. The severity of glaucoma was grouped as mild, moderate, and severe using the Canadian glaucoma staging system (10).

Data quality control and analysis

After the evaluation of each patient, a diagnosis for each eye was identified and documented. The principal investigator revised each data for completeness and entered. Data management and analysis were done using the SPSS version 26.

Ethical considerations

Ethical clearance for this study has been obtained from the Research and Publication Committee of the Department of Ophthalmology, School of Medicine, College of Health Sciences, Addis Ababa Universit, Ref Number MF/OPH/146/20 date 06/04/2020. Informed consent was obtained from each participant. Confidentiality and privacy were maintained. All individual identifiers were omitted from the collected data.

Result

A total of 449 new patients were diagnosed as glaucoma or glaucoma suspects in Menelik Hospital during the study period. One hundred seventy-three (38.53%) had secondary glaucoma. Ninety-five (54.9%) were males, and seventy-eight (45.1%) were females with an M: F ratio of 1.2:1. The mean age at presentation was 57.47 ±14 years, ranging between 19 to 85 years (Table 1). The leading causes of secondary glaucoma were found to be pseudoexfoliative glaucoma (PXG) 75.5%, neovascular glaucoma (NVG) 7%, uveitic glaucoma (6.7%), lens-induced glaucoma (5%), and miscellane-

ous causes (5.7%). Miscellaneous causes include traumatic, steroid-induced, pseudophakic, post-keratoplasty, and aphakic glaucoma (Figure 1). The most common cause of secondary glaucoma in the age group between 18 and 40 years was uveitic glaucoma (UG) accounts for 48% of the cases. All post-traumatic and steroid-induced glaucoma cases were in this age group. Between the age group of 41 to 60 years and in the age group >60, the most common cause of secondary glaucoma was pseudoexfoliative glaucoma, accounting for 70.83% and 84.2% cases, respectively, followed by neovascular glaucoma and lens-induced glaucoma. Neovascular glaucoma was a significant cause of secondary glaucoma that affects all age groups, with 47% of the patients being in the age group 41 to 60 years. The most common secondary cause in males and females was PXG, accounting for 74.73% and 56.41% of cases, respectively. Intraocular pressure of examined 173 patients (298 secondary glaucoma eyes) ranged between 10 to 72 mmHg, averaging 30±15mmHg. It was identified that 60 glaucomatous eyes were on IOP-lowering medications, whereas the other ten eyes underwent trabeculectomy. The vision of 40 eyes was no light perception (NLP), and 111(37.3%) presented with visual acuity of <3/60 to LP (Table 2). The optic nerve was evaluated in 230(77.1%) glaucomatous eyes, of which vertical cup-to-disc ratio(VCDR) was >0.85 in 124(41.6%) eyes, 0.7-0.85 in 61(20.46%) eyes, <0.65 in 45(15.1%) eyes. In the rest of 68 (22.8%) eyes, fundus could not be visualized due to corneal oedema and scar, lens opacity, posterior synechiae, and vitreous opacity. Gonioscopy was possible to perform in 275 glaucomatous eyes (92.3%), and the angle was open in 238 (79.9%) eyes, while a closed angle was identified in 37 (12.4%) eyes. Due to different unconducive ocular conditions, doing a gonioscopy in 23 (7.7%) eyes was complex.

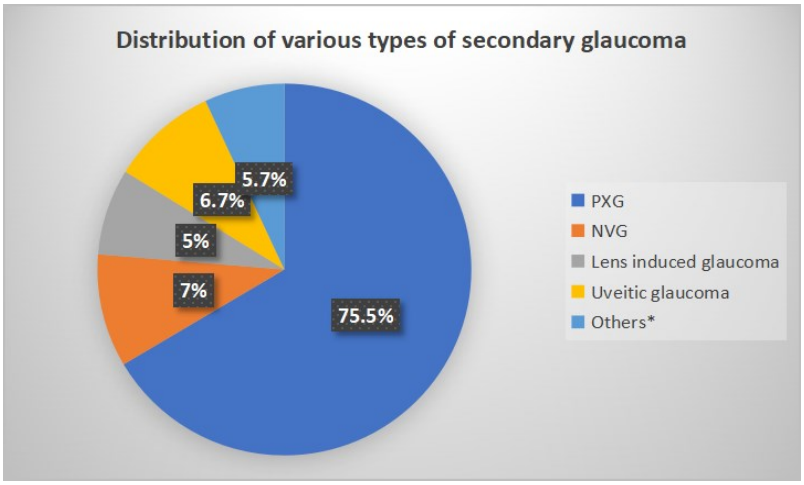
The majority of patients with secondary glaucoma were bilateral (69.4%), unilateral in 28.3%, and 2.3% (5 patients) had different types of secondary glaucoma in each eye, of whom four patients had PXG in one eye and NVG in the fellow eye. In contrast, one patient had uveitic glaucoma in one eye and NVG in the other eye. All cases of steroid-induced glaucoma were bilateral, whereas all post-traumatic were unilateral. The majority of NVG cases (64.7%), post-uveitic (84.6%), and lens-induced glaucoma (75%) were unilateral, whereas 89.1% of PXG patients were bilateral.

Pseudoexfoliative glaucoma constituted 75.5% of all cases of secondary glaucoma. Two hundred twenty-five eyes of 119 patients were affected by PXG, and the affected patients' age ranged from 46-85 years. It was bilateral in 106(89.1%) patients and unilateral in 13(10.9%) patients. One hundred five (46.7%) eyes presented with a best corrected visual acuity (BCVA) of <6/ 60. Eighty-two (36.4%) eyes presented with an IOP >30 mm Hg. Optic nerve head evaluation showed a cup-to-disc ratio of ≥0.7 in 156 (69.3%) eyes. On gonioscopy, 214 (95.1%) eyes had open angles, whereas closed angles were present in 4(1.8%) eyes, and evaluation was difficult in 7(3.1%) eyes due to corneal oedema related to high IOP. Among the examined patients, 225 eyes were found to have pseudoexfoliation material. PXF was identified at the pupillary margin in 61 eyes, the anterior lens capsule in 8 eyes, and the pupillary margin and anterior lens capsule in 156 eyes. Among PXG patients, five (4.2%) patients had the subluxated cataractous lens, which was bilateral in three, whereas the other four (1.8%) patients had associated retinal vein occlusion. Pseudoexfoliative glaucoma was more common in males (61.3%) than females (38.7%). Fifty-two (43.7%) patients reported known chronic medical illnesses, of whom 39 were hypertensive, six were diabetic, five were both diabetic and hypertensive, and the other two were asthmatic. Neovascular glaucoma constituted 7% of cases of all secondary glaucoma. Twenty-one eyes of 18 patients were affected by NVG. Unilateral NVG was present in 15 (83.3%) patients, whereas bilateral in three (16.7%) patients. All eyes presented with either NLP (61.9%) or LP (38.1%). Nineteen eyes (90.5%) presented with an IOP >30 mmHg. Optic nerve head evaluation showed a VCDR of ≥0.9 in six (28.6%) eyes, whereas it was not evaluated in the rest due to poor visualization of the posterior segment. On gonioscopy, eleven (52.4%) eyes had closed angles. In contrast, open-angle was present in one (4.8%) eye, and gonioscopy was not done in eight (38.1%) eyes due to corneal oedema related to high IOP. Among the NVG patients, four were diabetic patients with proliferative diabetic retinopathy, four were known hypertensive patients, of whom one had ischemic central vein occlusion, and the rest had no known ocular or systemic disease. Secondary glaucoma due to uveitis constituted 6.7% of all the cases. Most patients were between 18 to 40 years of age. Twenty eyes of 16 patients have been affected, of which 61.9% were unilateral cases. Females were affected more (1:2.2). Most patients had recurrent anterior uveitis (81.3%), and the rest had recurrent panuveitis. At presentation, 19 eyes (95%) had visual acuity of <6/60, thirteen eyes (65%) had an IOP>30 mmHg, and 45% had a cup-to-disc ratio of ≥0.7. It was impossible to evaluate the rest due to poor posterior segment visualization. Gonioscopy showed closed angles in sixteen eyes (80%), and the rest two had open angles, whereas the remaining two were not evaluated due to corneal oedema related to high IOP. Associated posterior synechia was present in most of the eyes.

Lens-induced glaucoma constituted 5% of all the cases of secondary glaucoma, affecting patients mainly in the age group of >40 years (84.6%). Fifteen eyes of 13 patients were affected, of which 84.6% were unilateral. All the patients presented with visual acuity of <6/60, and fourteen eyes (93.3%) had IOP>30 mmHg. 12(80%) eyes presented with phacomorphic glaucoma, whereas the other three were related to the subluxated cataractous lenses. The hazy view made the posterior segment impossible to see in all cases. Miscellaneous causes

Table 1: Socio-demographic characteristics of newly diagnosed secondary glaucoma patients. Menelik Hospital, Addis Ababa, Ethiopia, 2022.

Patient Characteristics	Categories	n (%)
Gender		
	Male	95 (54.9)
	Female	78 (45.1)
Age		
	18-40	25(14.5)
	40-60	72(41.6)
	>60	76(43.9)
Marital status		
	Single	11(6.4)
	Married	130(75.1)
	Divorced	17(9.8)
	Widowed	15(8.7)
Residence area		
	Urban	92 (53.2)
	Rural	81 (46.8)
level of education		
	Illiterate/no formal education	90 (52)
	Elementary School (1-8)	51 (29.5)
	High School (9-12)	20 (11.6)
	Diploma and /or above	12 (6.9)
Current occupation		
	Government employee	10 (5.8)
	Private/self-employee	33 (19.1)
	Daily labor	5 (2.9)
	Housewife	25 (14.5)
	Student	7 (4.0)
	Farmer	64 (37.0)
	Retired	29 (16.8)



Pseudoexfoliative Glaucoma (PXG), Neovascular Glaucoma (NVG)
Fig 1: Distribution of various types of glaucoma. Menelik Hospital, Addis Ababa, Ethiopia.2022.

constituted approximately 5.7% of all the cases of secondary glaucoma. These include traumatic (4 eyes), steroid-induced (6), pseudophakic glaucoma (3), post keratoplasty (3), and aphakic glaucoma (1).

Table 2: Presenting best corrected visual acuity of secondary glaucoma. Menelik Hospital, Addis Aba-ba, Ethiopia. 2022.

Best-corrected visual acuity	**Right eye**		**Left eye**	
	N	%	N	%
NLP	25	(14.5%)	15	8.7%
LP	35	(20.2%)	27	15.6%
CFI	11	(6.4%)	13	7.5%
<3/60-CFI	10	(5.8%)	15	8.7%
<6/60-3/60	10	(5.8%)	11	6.4%
<6/18-6/60	24	(13.9%)	31	17.9%
<6/12-6/18	19	(11%)	20	11.6%
≥6/12	39	(22.5%)	41	23.7%
Total	173	100%	173	100%

Discussion

This study provides information on various causes of secondary glaucoma presented to a tertiary eye hospital in Ethiopia. The secondary glaucoma study accounted for 38.5% of all new glaucoma cases during the study period, and it is comparable to a study done at the same hospital 13 years back, which identified 26.6% of patients with PXG and 14.3% with other secondary glaucoma (11). The previous studies did not mention secondary glaucoma subtypes, and pediatric age groups were included. This study has shown that the leading causes of secondary glaucoma were found to be pseudoexfoliative glaucoma (75.5%), followed by NVG (7%), uveitic glaucoma (6.7%), and lens-induced glaucoma (5%). PXG was disproportionately common in this study, which aligns with the previous reports, ranging from 11.3% to 35.2% for all sub-types of glaucoma in different parts of Ethiopia (12). Clinic-based reports of pseudoexfoliative glaucoma in other parts of Africa vary from no known reports in Ghana to a prevalence of 19% in South Africa (13). The higher prevalence is also reported in Finland, Iceland, Sweden, and other Scandinavian countries (14). The reason for this variation is unclear; environmental, geographic, genetic, and dietary factors are incriminated to be responsible.

The leading cause of secondary glaucoma was PXG, followed by NVG and uveitic glaucoma in this study, similar to the study done in Saudi Arabia (15). In comparison, other authors (3,8,14,16) found different common subtypes of secondary glaucoma. The prevalence of secondary glaucoma varies globally from 0.2 to 26.7% among various studies with varied etiologies (3,7,15–17). These variations in different studies might be due to differences in socio-demographic characteristics, study design, patient awareness, and availability and quality of ophthalmic services. The profile of secondary glaucoma is also changing with improved surgical practices, increased awareness among people towards ophthalmic services, increased life expectancy, and application of various preventive measures (6)

In this study, males were affected more frequently with secondary glaucoma (55%) compared to 45% of females. Likewise, it was reported that more males were affected in a study conducted in India(8). On the other hand, more females were affected, as reported in other studies(15-17). This dominance in females could be partly due to variations in the common subtypes of secondary glaucoma or other unknown factors. In the present study, males (61.3%) were affected by PXG more than females (38.7%). There were varying reports on gender predilection for pseudoexfoliative glaucoma in Africa (3,10,11). We acknowledge that it is not easy to know whether PXG is more common in males, as reported in this study, or whether the difference is due to the variation in health-seeking behavior between males and females. In our study, most cases of secondary glaucoma were bilateral (64.5%), contrary to other studies that reported unilateral secondary glaucoma as the most common (7,14). This could be due to PXG being the most typical cause of secondary glaucoma in the index study, a primarily bilateral disease with asymmetric involvement of both eyes. There were lower frequencies of post-surgical glaucoma, which might be explained partially due to the absence/ limited availability of the surgeries, as is the case for posterior segment surgeries, or due to improved surgical services and follow-up of post-surgical patients.

Secondary glaucoma was a significant cause of visual morbidity, with 57.7% of eyes presenting with BCVA <6/60, IOP >30mmHg in 45.3% of eyes, and 61.74% with a VCDR of ≥0.7 on presentation. It could be higher than this as there were cases in which the posterior segment was not visible, mainly due to media opacities. Their poor clinical profile could have contributed to a higher percentage.

Conclusion

Secondary glaucoma was a significant cause of visual morbidity and results from various identifiable ocular or systemic disorders. The underlying cause usually overshadows the features of associated secondary glaucoma, so the diagnosis is often overlooked, and management is delayed. Pseudoexfoliation remains the most common identifiable cause of secondary glaucoma, and most patients presented at an advanced stage with irreversible vision loss. Therefore, we recommend creating awareness about this disease and sharing details about emerging information of its risk factors to be explored.

Limitations of the study

The study was conducted in a tertiary eye care centre where most advanced and complicated cases are seen. Thus, mild to moderate cases could be treated in primary and secondary eye care centres, or they might not seek health care. Additionally, this study was a single-centre study with small study participants and mainly reflected the magnitude of secondary glaucoma in tertiary ophthalmic centres of Ethiopia. The proper visual field test was not performed as the Humphrey Field Analyzer was not available in our setup during the study period.

Competing interests

There is no competing interest to declare.

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Authors' contributions

All authors have approved the final version of the manuscript. AMA participated in the research proposal preparation, analysis, and writing of the data manuscript. GTG wrote the proposal, collected data, analyzed it, and wrote the manuscript.

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Original Article

Practicality of Frozen Section at Tikur Anbessa Specialized Hospital: A Pilot Study

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Abstract

Background: *Frozen section is an intraoperative rapid diagnostic tool that could direct a patient's intra- or post-operative therapy. Given the importance of frozen section in the management of surgical patients and the lack of published research in Ethiopia, it is prudent to evaluate its efficacy in our setting.*

Methods: *A prospective diagnostic accuracy study was done on 39 samples from June 2022 to December 2022. Cases were selected based on suspicion of a neoplasm and where there was an indication to perform frozen section. Data analysis was conducted using SPSS version 23. Findings were demonstrated using text, charts and diagrams.*

Results: *The accuracy, sensitivity, specificity, positive predictive value, and negative predictive value of frozen section as opposed to histopathological diagnosis using paraffin-embedded samples was found to be 92.3%, 88% and 95.2%, 94.1%, 90.9%, respectively. The mean turnaround time for frozen section was found to be 23 minutes.*

Conclusion: *The accuracy, ability to detect true positive cases, and ability to exclude false-positive cases of frozen section diagnosis in this research are consistent with most worldwide quality assurance data for frozen section. Despite its constraints, frozen section is a highly dependable method when carried out by experienced personnel, in the study context.*

Keywords: *Frozen section, Intra-operative Consultation, Accuracy, Sensitivity, Specificity, Ethiopia*
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Introduction

The practice of examining tissue removed by surgery pathologically did not become standard until the late 19th and early 20th centuries (1). Clinicians had limited resources aside from the patient's medical history and physical evaluation to assist in identifying neoplasms. Over time the use of x-ray and CT scan have helped in the diagnosis of malignant tumors. Despite advanced technologies, a definitive diagnosis would still need histopathology (1).

Assessing tissue obtained after operation following formalin fixation of the excised tissue usually takes days. In specific situations, surgeons need immediate histopathologic diagnosis during surgery to make intra -operative decisions. As a result, they order frozen section diagnoses (2, 3, 4).

Frozen section (FS) is an intraoperative examination of a tissue, which aims at histologically assessing small fragments of tissue in which there is a diagnostic doubt (5). FS offers quick diagnoses for directing patient care during surgery, including identifying unknown pathological conditions, assessing surgical margins, detecting lymph node metastases, and determining tissue type (4). FS should not be treated as an emergency procedure due to the practical aspects of the procedure that require preparation and the availability of the technician at the time of the operation. Therefore, an appointment at least a day before the operation needs to be made with the pathologist (4). Periodic reassessment of FS diagnosis by comparing it with the final diagnosis is valuable for pinpointing potential errors and preventing

their recurrence (3). The correlation of intra-operative FS diagnosis with final diagnosis on permanent section, formalin fixed paraffin embedded (FFPE) tissue, is an integral part of quality assurance in surgical pathology (6). Most studies indicate a frozen section accuracy of over 90%, with variation based on the specific organ being analyzed (5). Reasons put as the main causes for discrepancies were either misinterpretation of the original FS (31.8%), absence of diagnostic tissue in the frozen material but present in the un-sampled tissue or in the corresponding permanent section (31.4%) (6,7). FS serves as a rapid tool for guiding intra- or peri-operative patient management, but it does not supplant FFPE tissue technique. Its restrictions, such as limited sampling and technical challenges in obtaining high-quality tissue, affect the pathologist's interpretation of the section (1). The method remains dependable when performed by skilled practitioners. In Ethiopia, the use of FS as intraoperative consultation is near to zero. The Department of Pathology at School of Medicine, College of Health Sciences (CHS) is in preparation to start this procedure at Tikur Anbessa Specialized Hospital (TASH). This pilot investigation seeks to establish the practicality and accuracy of frozen section analysis in Ethiopia, as there is significant lack of research on this topic in the country. It will be the first research of its kind and serve as a foundation for future studies in this area.

Methods and materials

Study design

A pilot study on the diagnostic accuracy of FS carried out at the Department of Pathology, CHS at TASH, Addis Ababa, Ethiopia. A prospective diagnostic accuracy pilot study of intraoperative
FS specimens sent to the department from June 2022 to December 2022 were included. The project was initiated at the Department of Pathology, CHS, TASH, Addis Ababa, Ethiopia as it receives pathology specimens from all over the country providing large-scale pathology-based data (8).

Study population

Patients undergoing surgery having an indication for frozen section due to suspicion of a neoplasm were further selected, after which study population was chosen according to the eligibility criteria.

Eligibility criteria

All specimens sent to the pathology department for FS analysis were included in the study. Samples with inadequate tissue for diagnosis, samples with no follow up resection specimen, cases from emergency operation, and patients with age less than 18 years due to difficulty of obtaining parental consent for a practicality study were excluded from the study.

Sample size determination and sampling technique

In determining the sample size for this study,the rule of thumb was utilized, taking into consideration the fact that pilot studies need a minimum of 30 samples or greater to estimate a parameter (9). Samples were collected based on suspicion of a neoplasm and an indication to conduct FS including clinical features, the presence of potential contributing factor or result of preceding test (10).

Data collection procedure

Intraoperative FS specimens sent to the department from June 2022 to December 2022 were included. Intraoperative tissue was transferred to the pathology department in normal saline, and the time of sample receipt was recorded. Representative sample was taken to the cryostat machineand frozen at -25°C. Slides were prepared for evaluation by two senior pathologists and an expert pathologist. Findings were reported to the surgeon while still in surgery. After the frozen section procedure, both frozen and any remaining non-frozen tissue were preserved in a 10% formalin solution and forwarded to thehistopathology lab for creating permanent paraffin-embedded sections. FFPE slides were again further evaluated by two senior pathologists and one expert pathologist (Flow diagram 1). Upon comparing the FS report provided during surgery with the final histopathology report of the FFPE sections, the accuracy rate, sensitivity, and specificity of the FS reporting were evaluated (2,11). Using SPSS 23, data were statistically analyzed, and evaluation of sensitivity, specificity, positive and negative predictive values of the test was conducted.

Ethical considerations

The study received ethical approval from the institutional review board (IRB) (028/22/Patho), confirming that ethical principles were followed. Patient anonymity was maintained throughout the research by using coded identifiers to ensure patient privacy. To protect data, strict safeguards were put in place, such as limiting access to authorized researchers, storing physical and electronic records securely, and anonymizing participant identification during data analysis and reporting.

Results

A total of 39 samples were collected. The age of patients ranged from 29 years to 68 years. Mostpatients (46.1%) were between the ages of 36 and 45 (Table 1). 35 (89.7%) patients were femalewhile the rest 4 (10.3%) of the patients were male (Table 1).

Table 1: Patient demography and turnaround time for FS, Addis Ababa, Ethiopia (n=39)

		Count
Age groups	26-35 years	10
	36-45 years	18
	46-55 years	6
	56-65 years	4
	>66 years	1
Sex	Female	35
	Male	4
Turnaround time	≤20 minutes	19
	21-35 minutes	12
	26 -30 minutes	7
	31-35 minutes	1

Table 2: Specimen body sites and indication for FS, Addis Ababa, Ethiopia

		Indication for frozen section				**Total**
		Primary diagnosis	LN metas-tasis	Local Me-tastasis	Margins	
Specimen body	Ovary	7	0	1	0	8
	Omentum	0	0	5	0	5
	Lymphnode	0	10	0	0	10
	Breast	0	0	0	3	3
	Colon	1	0	0	1	2
	Fallopian tub	0	0	1	0	1
	Cervix	3	0	0	0	3
	Uterus	6	0	0	0	6
	Mesentery	1	0	0	0	1
Total		18	10	7	4	39

Assessment of primary diagnosis was the most common reason for FS accounting for 46.2% (18) of cases, followed by assessments of lymph node metastasis(10) (25.6%), local metastasis (7) (17.9%), and margin evaluation (4) (10.3%).

Among the collected specimens, the majority were lymph nodes (10) (25.7%), followed by ovary, parametrium, omentum, cervix, surgical margin, colon, fallopian tube, and mesentery (Table 2).

The entire FS procedure took anywhere between 20 and 35 minutes, from the time the specimen was out of the operation room to the time the FS diagnosis was relayed to the attendingsurgeon. In most of the cases (19) (47.5% of cases), the time it took to reach diagnoses was 20 minutes (Table 1). In general, the diagnosis of FS took an average of 23 minutes.

Of all FS samples evaluated, 51.3% (20) were negative for neoplasm and 43.6% (17) of samples were positive for neoplasm. Two samples had indeterminate results (5.1%) as it was difficult to give conclusive diagnosis due to poor staining and sampling. (Flow diagram 1)

Negative for neoplasm samples were further classified as reactive lymph node (8) (40%), unremarkable omentum (5) (25%), free margin (4) (20%), unremarkable ovary (2) (10%), and unremarkable mesentery (1) (5%).

The most common type of neoplasm detected was Leiomyoma (6) (35.2%), followed by benign ovarian cyst (4) (23.5%). Two samples (11.7%) were diagnosed as suspicious for malignancy, two lymph nodes (11.7%) as secondaries of carcinoma, one sample (5.8%) as mucinous neoplasm, one sample (5.8%) as sex cord stromal tumor and one cervical punch biopsy (5.8%) as Invasive squamous cell carcinoma.

Of the 39 FS samples, 3 (7.7%) were discordant while the rest 36 (92.3%) samples were concordant with FFPE section diagnosis. From the discordant samples, one case diagnosed as positive for malignancy ended up being negative for malignancy during FFPE sectioning, which was counted as false positive. The two indeterminate results were classified as false negative as FFPE section slides showed positive for malignancy; the diagnosis for both was invasive squamous cell carcinoma. This classification of putting indeterminate result as false negative was based on a conservative approach assuming 'worst case scenario' (12).

Table 3: Cross tabulation of FS and FFPE section results of samples sent, Addis Ababa, Ethiopia (n=39)

FS diagnosis	**FFPE tissue diagnosis**	
	Positive for Neoplasm	Negative for Neoplasm
Positive for Neoplasm	16	1
Negative for Neoplasm	2	20

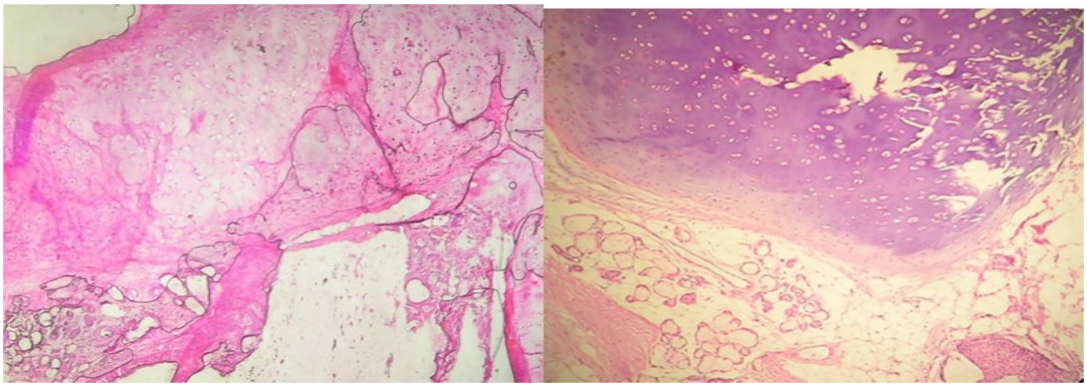
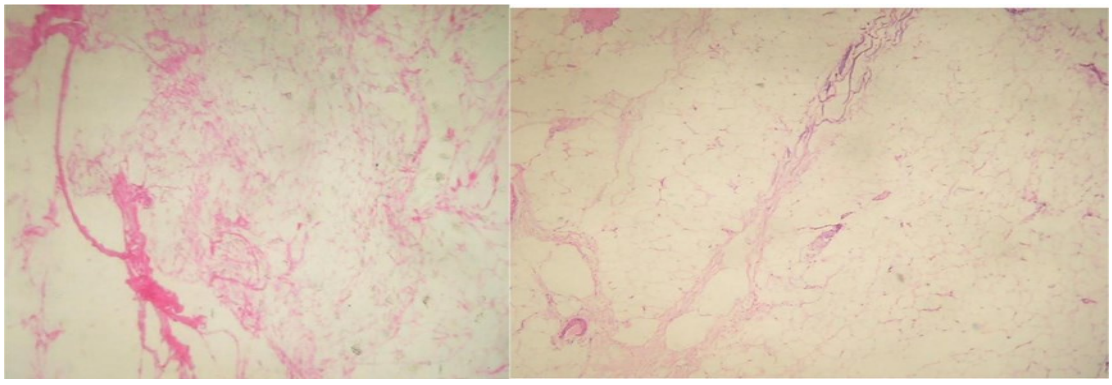
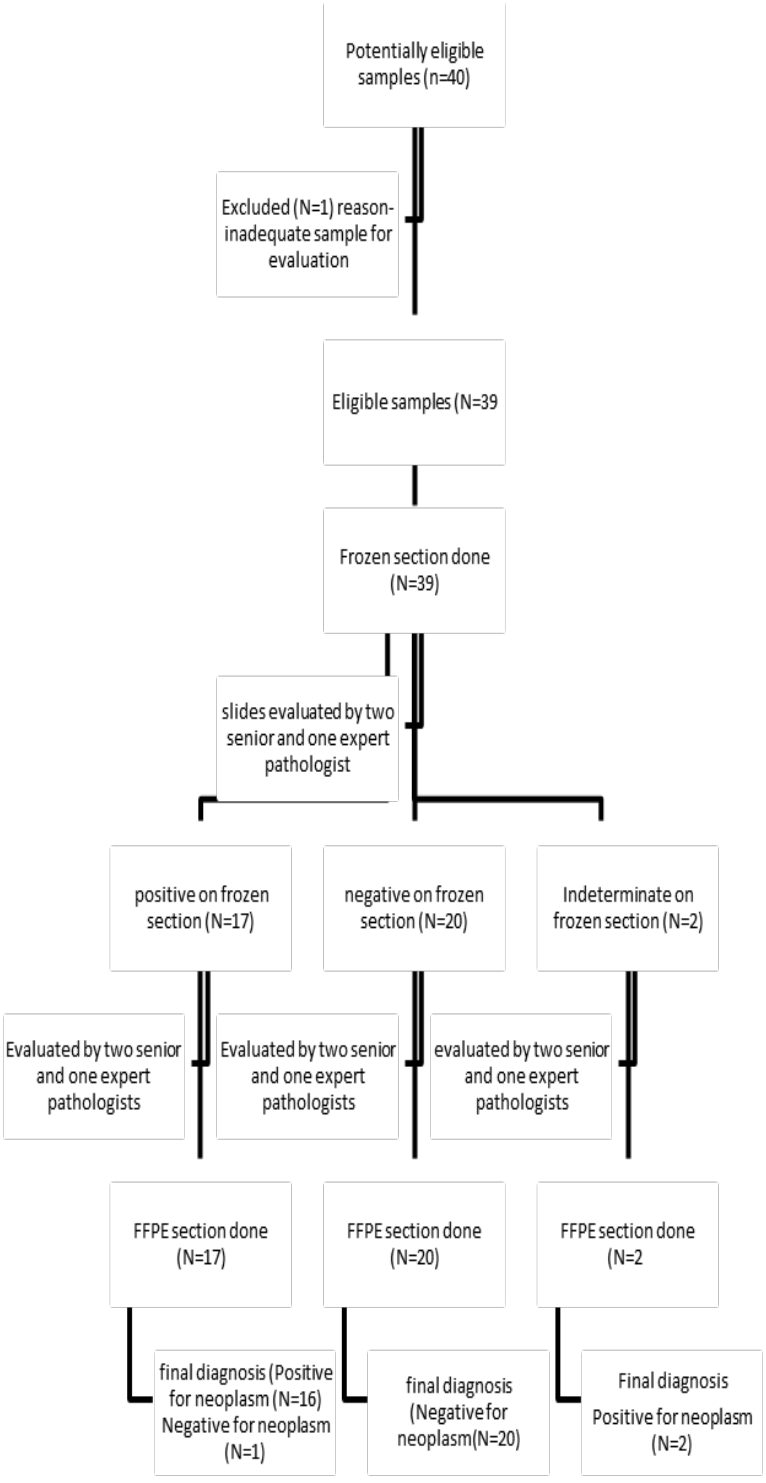


Figure 1: A. (Left, 20x magnification). FS (HE stained slide) of a mature teratoma. B. (Right, 20x magnification)



FFPE (HE stained slide) of a mature teratoma.



Flow Diagram 1: Sample identification and processing workflow

Overall concordance rate was 92.3% (N=36) with 3 (7.7%) discordant cases. All the discordant cases were due to technical error, specifically bloating of cells on FS and poor staining quality. It was determined that FS has a sensitivity of 88% and a specificity of 95.2%. Findings showed that FS had a 90.9% positive predictive value and a 94.1% negative predictive value when it came to identifying neoplasms.

Table 4: Comparison of various studies with the present study on overall accuracy, sensitivity and specificity

Studies	Country	Number of specimens	Accuracy	Sensitivity	Specificity
Present study	Ethiopia	39	92.3%	88%	95.2%
Tangde A et al. (3)	India	83	91.57%	85.7%	97.9%
Gudeli Vahini etal.(11)	India	21	91%	90%	-
Hatami H et al. (13)	Iran	306	97.9%	92.9%	99.5%
Laila C et al. (14)	Morocco	14,000	95%	-	-
Santana RP et al. (5)	Brazil	1,226	96.3%	-	-
Chandramouleeswar i K et al. (15)	India	51	92%	-	-

Discussion

This study looks at common indications for FS, turnaround time, accuracy, and causes ofdisagreement in FS diagnosis. The findings show that primary diagnosis and lymph node involvement are the two main reasons for FS diagnosis request in our setting. The frequently sampled sites are lymph nodes and ovaries. The study also highlights the importance of a timely turnaround time in FS diagnosis. The accuracy rate of 92.3% aligns with previous research, supporting the reliability of FS. Discrepancies between FS and final histopathological reports areattributed to technical errors, which was also the case in other similar studies. Most common indication for FS in our study (Table 2) was similar to other studies (2,3,16,17). Both pathologists and operating surgeons should be fully aware of the indications for FS to guarantee that the right requests are fulfilled. Errors can only be decreased after that (14,18,19). In this study lymph nodes and ovaries were determined to be the anatomical areas most frequently sent for FS diagnosis (46.1%) (Table 2), which was also the case in most other studies (5,16).

The turnaround time, described as the span of time from the moment the sample was received until the surgeon received the report, should not exceed 30 minutes. In our study 97.4% of samples were diagnosed within the proposed turnaround time, which was similar to studies donein India (16,20). One sample, a lymph node, which was the first one processed in this study, took 35 minutes to process, which could be explained by the time needed to become familiar with the cryostat system. This finding shows that it is feasible to do FS in our setting within the proposed time.

Our study showed an accuracy rate of 92.3%. This finding aligns with similar studies (Table 4), Based on the kinds of cases they examined, most centers reported accuracy rates ranging from 92% to 98% (21). Accuracy rate has shown to be more than 90% (2). Several studies have found a clear relationship between sample size and FS accuracy (Table 4). The accuracy of FS appears to rise as sample size increases, which is why a plan to do a larger study in the same setup is necessary. In this study, sensitivity was found to be 88%, while specificity was found to be 95.2%.We found that the sensitivity was lower than the specificity when it comes to identifying neoplastic cases, which is consistent with most researches (13,15,22). Higher specificity can be explained by the fact that the rationale for FS in our investigation was to rule out the existence of malignancy. Consequently, this study demonstrated that FS can be used to exclude malignancy, hence limiting the extent of the operation.

Technical error was determined to be the possible reason for the discrepancy between theintraoperative FS and the final FFPE histopathological report. This finding agrees with other studies which showed that causes for discordance were broadly classified as sampling error, technical error, and interpretative error in various studies (3,11,17,21). Sample error encompasses inadequate tissue sampling as well as inappropriate tissue selection subsequent to grossing.

A substandard section, Xylene/freezing artifact, bloated cell structure, and poor staining were among the technical issues (11). In our study bloated cell morphology and poor staining were the main causes which resulted in discordant cases. This finding can be explained by the relative inexperience in doing FS in the department. Hence, refining technical aspects of FS is believed to increase the accuracy rate.

Since this was the department's first attempt at implementing FS, there have been technical obstacles and a learning curve involved with the work. Ongoing training and quality improvement efforts may aid in

overcoming these restrictions. Due to the nature of this pilot study, which primarily focused on assessing the feasibility of FS, long-term follow-up data including patient outcomes and treatment success rates were not included. This limitation arises from ethical considerations concerning the decision -making process during surgical operations. Thus, surgeons were specifically instructed to base treatment decisions on their clinical judgment rather than only on the FS diagnosis provided. The relationship between FS diagnosis and patient outcomes would need to be examined in further research with a bigger sample size and longer follow-up.

Conclusion

FS was found to have 92.3%, 88%, and 95.2% accuracy, sensitivity, and specificity when compared to FFPE tissue diagnosis which are comparable with most international studies on FS. Given that this is a pilot study, a larger investigation should be carried out to use these findings as a benchmark. As the turnaround time was within the standard, FS results, particularly in institutions with trained pathologists, can be used to guide the type and scope of operation.

Increased diagnostic accuracy can be achieved through more precise and larger sampling, avoidance of sectioning errors, accurate interpretation, and knowledge of clinical history and presentation. We recommend forming and communicating with a multidisciplinary team that includes operating surgeons, on-call pathologists, and technicians, so as to decrease diagnostic errors. Despite its technical errors, the FS approach is very dependable and efficient in the right hands.

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Authors contribution

MD primarily led the conception and design of the research in addition to conducting the statistical analysis and preparing the initial manuscript. SA and AD played vital roles in contributing to the study's conception and providing valuable input during manuscript review. WE carried out the pathologic interpretation of the collected samples, ensuring accurate data interpretation. BS and VA were responsible diligent collection of research data. Throughout the process, all authors actively participated in revising the manuscript, incorporating feedback and suggestions, and ultimately approving the final version.

Competing interests

The contributors assert to have no known conflicts of interest.

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Data availability

All necessary data is obtainable upon plausible request.

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Original Article

Duplex Doppler Assessment of Portal Vein Congestive Index in Asymptomatic Hepatitis B Virus infected Patients in a Resource Limited Set-up: A Case-Control Study

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Abstract

Background: *A good number of patients with viral hepatitis are asymptomatic and detected as incidental findings. Early detection of the hemodynamic changes as well as prompt treatment is paramount to prevent the development of complications such as portal hypertension, liver cirrhosis and hepatocellular carcinoma. The congestive index (CI) of the portal vein has a high sensitivity and specificity in the diagnosis of hepatic fibrosis and portal hypertension and it is therefore imperative to assess these categories of patients using this index. The objective of this study is to compare the portal vein CI of patients with asymptomatic hepatitis B viral infection and normal individuals"*

Methods and Patients : *This is an institution-based case-control study comprising 112 cases with serological diagnosis of hepatitis B viral infection and 112 age and sex-matched controls that were seronegative for hepatitis B and C viral infection and had normal LFT parameters. The CI of the participants were obtained using duplex Doppler ultrasound, and the data obtained were analyzed using statistical package for social sciences (IBM SPSS version 23.0. Armonk, NY).*

Result: *224 participants made of 112 cases and 112 age and sex-matched controls were evaluated. The age of the participants ranged from 18-63 years. 113 (50.4%) of the participants were males, while 111 (49.6%) were females. The mean value of the portal vein CI was 0.04±0.003cmS among controls and 0.06±0.01cmS among cases; however, the difference was not statistically significant (p 0.192). CI was noted to increase with age and was higher among the male gender, but the difference was also not significant statistically. Also, LFT parameters among the participants was higher in cases than the control and most were statistically significant except for ALP and AST.*

Conclusion: *The CI of the portal vein and LFT parameters were higher in cases than control and and it may therefore be a useful tool in the assessment of patients with hepatitis, particularly in symptomatic cases.*

Keywords: *Portal vein, congestive index, asymptomatic hepatitis B virus patient*
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Introduction

Infection with hepatitis B is a serious health challenge to the general public. About 2 billion people worldwide have hepatitis B viral infection and 350 to 400 million have chronic hepatitis B viral infection with about 620,000 dying annually.[1] Hepatitis B viral infection is endemic in many continents including Africa, and Nigeria has a very high prevalence of 12.2%.(2,3)

Most patients with viral hepatitis are asymptomatic and can present this way for years and even decades. The presentation could be mild and may not cause significant liver disease, but in some patients, there could be continued inflammation which can lead to fibrosis, hepatic steatosis, cirrhosis, liver failure and liver cancer.[4] It is an established fact that progression of liver disease is accompanied by histological changes of the hepatic parenchyma such as hemodynamic changes, inflammation, necrosis, and fibrosis.(4,5)

Hepatitis B surface antigen (HBsAg) is the investigation of choice for screening for HBV infection. (6) Although about 15% to 40% of hepatitis B virus carriers will develop hepatic complications such as cirrhosis, hepatic decompensation and hepatocellular carcinoma, most patients will remain asymptomatic.(7) The vascular complication that could arise from chronic viral hepati-

tis include portal hypertension with or without porto-systemic shunts, flow changes in the hepatic artery and vein, thrombosis of the portal vein, and neovascularization of liver tumour. (8) The severity of the changes involving the hepatic vasculature depends on the degree of fibrosis progression. (9)

Evaluation for liver fibrosis is essential in monitoring patients with asymptomatic chronic hepatitis B viral infection, to assess the progression of liver disease, and this determines when to institute drug therapy. Liver biopsy is still considered the gold standard, but it is an invasive procedure associated with risks and mis-classifications which is not well accepted by patients, making it unsuitable for regular follow-up examinations. This has over the years led to investigations with non-invasive modalities such as transient elastography and portal vein congestive index. (8,9) Transient elastography is particularly preferred to liver biopsy for diagnosis and follow-up examinations of fibrosis but more hands-on training and availability of the needed software will be necessary to make it more effective in our setting.

Grey-scale ultrasonography of the liver may provide important findings related to parenchymal changes in patients with viral hepatitis especially when complications arise but it cannot assess hemodynamic changes hence, the need for Doppler assessment.(10) Due to the limitations associated with the different values from many Doppler parameters of the liver vasculature, researchers have used some new indices for more reliable evaluations such as portal vein congestion index, modified hepatic index (MHI), arterioportal ratio and portal hypertension ratio.(10)

Various parameters have been used to evaluate the portal vein including diameter, cross sectional area, pulsatility index, mean flow velocity and congestive index but the latter is the most reliable, sensitive and specific parameter.(9,11-15) Assessing patients with this index will go a long way in averting the sequalae associated with viral hepatitis in our environment hence, the motivation for this study.

Methods

This prospective case-control study was carried out in the Radiology Department of University of Abuja Teaching Hospital following ethical approval by the Research and ethics committee of the institution. A total of 224 participants within the ages of 18 – 63 years made up of 112 cases and 112 controls were recruited. The cases were consenting asymptomatic adult patients with serological diagnosis of hepatitis B viral infection who met the inclusion criteria and referred to the Radiology Department for abdominal ultrasound scan from Internal Medicine and Family Medicine departments of the institution. The controls were consenting staff and students as well as eligible patients on medical check-up from the Family Medicine Department. The liver function test parameters of this category of patients were normal and they were also seronegative for both hepatitis B and C virus infections. Those excluded from the study were patients with obesity, renal diseases, liver diseases from other causes other than hepatitis. Pregnant women and lactating women as well as patients under 18 years of age were excluded from the study.

After obtaining an informed consent, the biodata and relevant clinical history were obtained to establish inclusion and exclusion criteria. Anthropometric measurements (height and weight) were obtained and BMI was then calculated using the formula Body Mass Index (BMI) = weight (kg)/height^2 (m^2). (16) About 5 milliliters (mls) of venous blood was then taken from all participants and the samples were evaluated at the Microbiology and Chemical Pathology Departments respectively for Hepatitis B and C screening using rapid test strips, and spectrophotometric assay for LFT parameters (bilirubin, total protein, albumin, liver enzymes [alkaline phosphatase, alanine transaminase and aspartate transaminase]). After ascertaining the eligibility of the participants, they were scanned with low frequency curvilinear probe (2.5MHz to 5.0MHz) on the Logic F8 expert GE (General Electric, USA 2016) colour Doppler ultrasound machine.

Following an overnight fast, the patients were asked to lie supine on the ultrasound couch, ultrasound coupling gel was applied on the abdomen and B mode grey-scale 2D ultrasound scan of the abdomen was performed. Using the right subcostal/intercostal approach, the entire liver was scanned in longitudinal, transverse and oblique planes, and the following parameters were evaluated: liver span, gall bladder wall thickness, longitudinal and transverse dimension of the gallbladder and the splenic length. The peritoneal cavity was also assessed for possibility of ascites.

The portal veins parameters (diameter, cross sectional area, mean flow velocity and then congestive index) were also evaluated at the level of the porta hepatis as shown in figures 1 and 2 below. The Doppler interrogation was done with Doppler angle of 60^0 with a sample size of 4mm-8mm. The mean flow velocity was calculated using $0.57Vmax/Cos\theta$.[9] The θ in this case was the Doppler angle 60^0 while the 0.57 was the correction factor of parabolic flow. Congestive index of the portal vein was then calculated by dividing the cross-sectional area by the mean portal vein flow velocity. All measurements were obtained twice and the average calculated to eliminate intra-observer variability

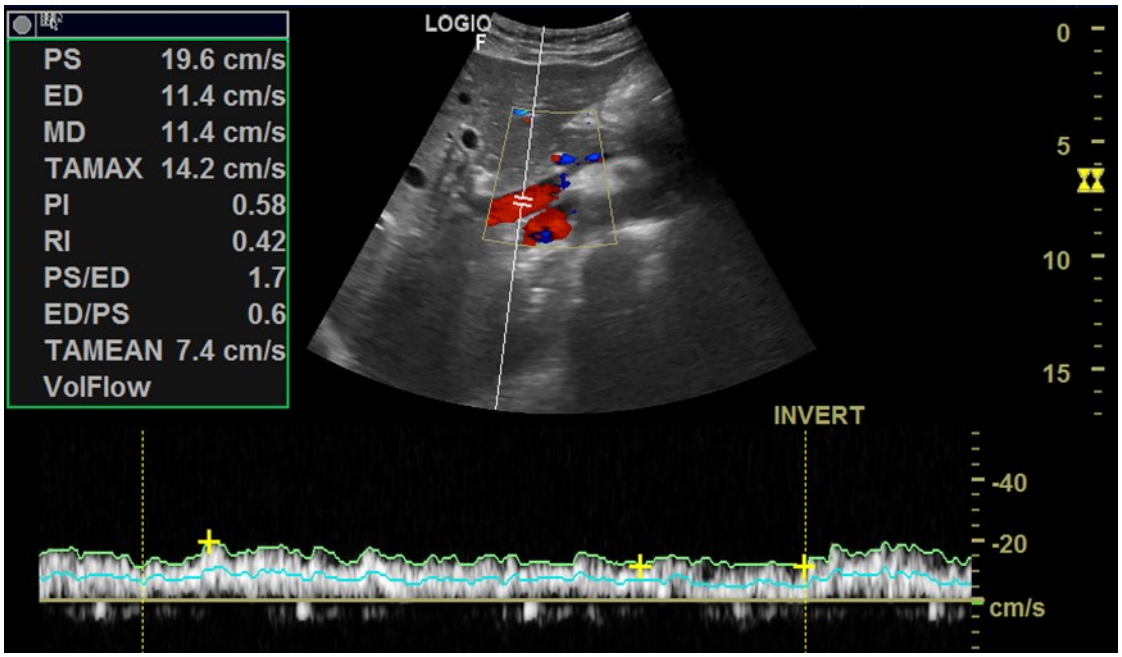

Figure 1: B -mode Ultrasound of the portal vein in transverse plane showing the cross-sectional area of the portal vein at the porta hepatis (1.01cm^2).

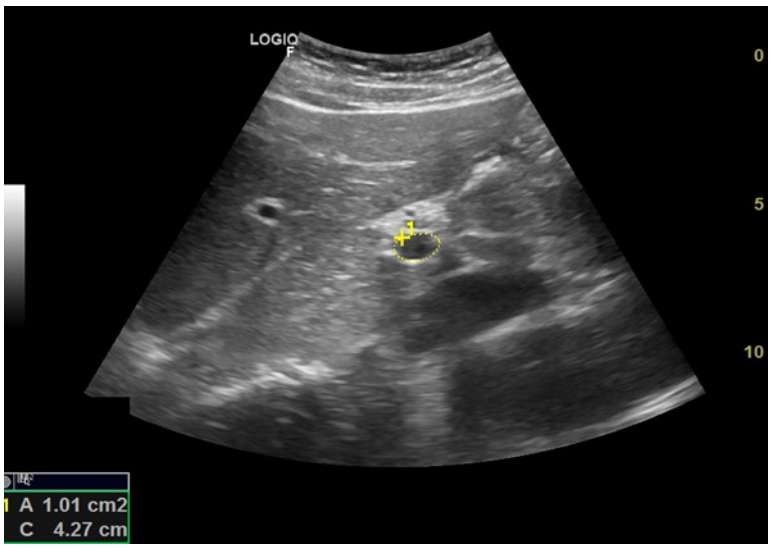

Figure 2: A duplex Doppler ultrasound scan of the portal vein at the porta hepatis demonstrating the normal spectral waveform of the portal vein (monophasic forward flow (hepatopetal) with mild respiratory phasicity and cardiac periodicity

Ethical considerations
Ethical approval was obtained from the Research Ethical Committee of the Hospital (No. UATH/HREC/PR/2018/012). The patients were provided with adequate counselling and care as appropriate and informed consent was obtained before their inclusion in the study.

Results
Data obtained from the 224 adult participants was analyzed with SPSS version 2021. Out of the study participants, 113 (50.4%) were males, while 111(49.6%) were females, with Male to Female ratio of approximately 1:1. This was comprised of 53(47.3%) males and 59(52.7%) females among the controls while 60(53.6%) males and 52(46.4%) females were in the case group as shown in Table 1. There was no statistically significant difference between gender (P = 0.350). The age of participants ranged from 18 to 63 years. The mean age for the controls was 36.47years ±10.72 years, while that of the cases was 36.75years ±9.78 years; and there was no statistically significant difference between the ages of the two groups (p-value 0.350). 34.8% of the controls and 37.5% of the cases were between 30-39 years of age, making it the largest age group in this study.

Table 1: Socio-demographic characteristics of respondents

Variables	Control (n=112)	Case (n=112)	χ^2/FET	p-value
Age (Mean±SD)	36.47±10.72	36.75±9.78	-0.202(t-test)	0.840
Gender				
Male	53(47.3)	60(53.6)	0.875	0.350
Female	59(52.7)	52(46.4)		
Total	112(100.0)	112(100.0)		
Age				
<20 years	3(2.7)	0(0)	3.434**	0.657
20-29 years	30(26.8)	28(25.0)		
30-39 years	39(34.8)	42(37.5)		
40-49 years	24(21.4)	28(25.0)		
50-59 years	13(11.6)	12(10.7)		
60-69 years	3(2.7)	2(1.8)		
Total	112(100.0)	112(100.0)		
Level of education				
None	1(0.9)	0(0)	5.029	0.136
Primary	2(1.8)	3(2.7)		
Secondary	10(8.9)	20(17.9)		
Tertiary	99(88.4)	89(79.5)		
Total	112(100.0)	112(100.0)		

*p-value significant at <0.05
** FET = Fisher's exact test

The mean weight among the control was 67.11kg ±8.34, while that among the cases was 67.45kg ±9.33 and there was no statistically significant difference between the two groups (p 0.774) as shown in Table 2.

There was a statistically significant difference between the BMI of the participants in the control and case groups (P 0.041) as shown in Table 2.

Table 2: Anthropometric distribution of respondents

Variables	Control Mean±SD	Case Mean±SD	t-test	p-value
Weight (Kg)	67.11±8.34	67.45±9.33	-0.287	0.774
Height (m)	1.65±0.07	1.69±0.09	-2.991	0.003*
BMI (Kg/m^2)	24.48±2.71	23.72±2.88	2.054	0.041*

**p-value significant at <0.05*

The liver function test parameters (Total Bilirubin, Direct Bilirubin, ALAT, Total Protein and Albumin) were found to be statistically different across the cases and control except for the ALP and AST of which showed no statistically significant difference as depicted in table 3. The mean value of Total Bilirubin and Direct Bilirubin were higher in cases than controls with a P value of 0.002 and <0.001 respectively. ALAT and Total Albumin were also higher in cases than control with a P value of 0.009 and 0.002 respectively.

Table 3: Comparison of Liver Function Tests among cases and controls

Variables	Control Mean±SD	Case Mean±SD	t-test	p-value
Total bilirubin	12.32±4.36	14.48±5.81	-3.153	0.002*
Direct bilirubin	4.86±2.33	6.20±3.08	-3.670	<0.001*
ALP	178.96±50.38	176.15±41.97	0.454	0.650
ASAT	23.73±12.11	25.21±10.15	-0.987	0.325
ALAT	22.93±9.94	27.34±14.58	-2.648	0.009*
Total protein	75.68±3.83	77.65±5.46	-3.128	0.002*
Albumin	44.25±3.47	46.16±4.19	-3.718	<0.001*

*p-value significant at <0.05

The grey-scale ultrasound findings and measurements of the liver, gallbladder and spleen of the participants were all obtained. The mean liver span was 14.58cm±1.39 and 14.24cm ±1.38 among controls and cases respectively. There was no statistically significant difference between the value of the liver span, gallbladder length, gallbladder breadth, gallbladder wall thickness and spleen size for the two groups, and the parenchymal echopattern of these organs in both groups was within limits of normal. The mean values for the portal vein cross-sectional area (PVCSA), mean flow velocity (MFV) and portal vein congestive index (PVCI) among control and case groups are as shown in Table 4. The aforementioned portal vein indices were found not to be significantly different across cases and controls.

The portal vein congestive index (PVCI) was higher among the cases with a mean value of 0.06 ±0.01cms as against controls with a mean of 0.04 ±0.026cmS. However, this was not statistically significant (p = 0.192). This is depicted Table 4. The PVCI among cases ranged between 0.010 to 1.100cms with a mean value of 0.056cmS ±0.01 while that among controls ranged between 0.010cmS to 0.0470cmS with a mean value of 0.040cmS.

Table 4: Comparison of sonographic findings of portal vein indices among cases and controls

Variables	Control Mean±SD	Case Mean±SD	t-test	p-value
PVCI	0.04±0.03	0.06±0.01	-1.311	0.192
VMAX	28.09±5.59	28.77±6.91	-0.812	0.418

**p-value significant at <0.05*

Association between PVCI and age among cases showed an increase in PVCI with increasing age as shown in Table 5. Also.,PVCI was higher in males than females (0.07cmS± 0.015 and 0.04cmS±0.006 respectively), but the differences that existed between them was not statistically significant (p = 0.292). The correlation analysis between PVCI and LFT parameters demonstrated weak positive correlations that were not statistically significant except for albumin which showed a weak negative correlation with no statistical significance

Table 5: Comparison of PVCI with age among cases using ANOVA

Variables	N	PVCI Mean±SD	F-value	p-value
Age grouping				
≤20 years	3	0.035±0.002	1.104	0.351
21-40 years	76	0.044±0.050		
41-60 years	32	0.087±0.199		
61-80 years	1	0.033		
Total	112	0.056±0.115		

*p-value significant at ≤ 0.05
**F = ANOVA value

Discussion

A total of 224 participants were included in the study, which comprised 112 cases and 112 controls that were age and sex-matched. The age of the participants ranged from 18 to 63 years with a mean age of 36.8±9.8 and 36.5 years ±10.7 among cases and controls respectively. The mean age among the cases is similar to that of the previous study carried out by Onyekwere and co-workers, (17) where the mean age of cases found to be seropositive for hepatitis B virus following a screening exercise was 36.1 ± 8.8 years. This shows that youths are more affected as Hepatitis is largely sexually transmitted and youths are more sexually active. Among the cases, there were more males 60(53.6%) than females 52(46.4%) which is also in agreement with the studies of Onyekwere and Baig where the prevalence of hepatitis B virus infection was found to be more in males. (17,18)

PVCI across age-groups among the cases showed an increase with increasing age as that connotes chronicity and possibly severity of the disease. Aiyekomogbon and co-researchers also demonstrated an increase in congestive index with increasing age in their study. (19) As the congestive index of the portal vein was higher in cases than controls, so also the values of all the liver function test parameters were higher in the cases when compared with the controls. These observations suggest that laboratory evaluation of liver function test and Doppler assessment of portal venous flow are sensitive in monitoring patients with asymptomatic hepatitis B virus infection who have normal clinical and grey-scale hepatic ultrasound scan findings. Congestive index of the portal vein is therefore a strong diagnostic parameter for early detection of subtle hepatic changes in patients with hepatobiliary disease. To the researchers' knowledge, correlation of PV congestive index with liver function test has not been studied previously in our immediate environment. A study done in Italy however established a strong positive correlation between alanine aminotransferase levels and transient elastography by Fibroscan in the evaluation of liver stiffness in hepatitis B virus carriers (t= 4.740, p-value <0.001), the alanine aminotransferase showed progressive decrease during antiviral therapy which paralleled the findings using transient elastography with Fibroscan.(20) This suggests that evaluation of the portal vein congestive index and correlation of its findings with those of liver function test may be beneficial in monitoring patients with hepatitis B virus infection.

recorded in the studies of other authors in Japan and Nigeria where they had respective mean values of 0.070cmS ±0.029 and 0.0722cmS ±0.0135. (9,19) The differences could be attributed to the inter-equipment and inter-observer variability. (21,22) Based on our observation, the congestive index of the portal veins for both groups were within limits of normal but those with viral hepatitis was higher than the control group. The normalcy recorded in the case group is anchored on the fact that asymptomatic hepatitis patients were considered and the higher value recorded for hepatitis patients as against the control in this study gives credence to the sensitivity of congestive index in the assessment of liver diseases and fibrosis. Subtle fibrotic changes may have taken place despite the fact that they were asymptomatic, bearing in mind that liver has high residual capacity. There was an increase in the mean value of the congestive index among the cases when compared with the control which is similar to the observation of other authors in Japan and India.(9.21) The difference found in the index study was however not statistically significant as the study was exclusively carried out among asymptomatic patients (P = 0.192). A previous study by Sato and co-researchers (23) revealed the mean values of congestive index as 0.007±0.028cmS in patients with chronic inactive hepatitis and 0.09±0.05cmS in patients with chronic active hepatitis and results obtained suggested that the congestive index which is a measure of the portal venous pressure and hepatic fibrosis began to increase at the stage of chronic active hepatitis. This study recruited only asymptomatic cases, thus unable to corroborate this PVCI finding in patients with advanced liver disease.

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Authors' Contribution

HM: Actively participated in the sonographic assessment of the patients and she also contributed substantially to the conception, design and writing of the manuscript

J.O.A: Contributed substantially to the conception, design and writing of the manuscript, and he is the corresponding author of the article.

U.D.I: made substantial input to the writing of the manuscript. She also reviewed and corrected the entire article before submission.

O.O.O: made substantial input to the writing of the manuscript. She also reviewed and corrected the entire article before submission.

K.H.O: Contributed substantially to the design and writing of the manuscript.

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Original Article

Grown, Chewed and Omnipresent, Catha Edulis Plant in Ethiopia, Its Livelihood Implication on Rural Households. Community Based Cohort Nutrition Study

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Abstract

Background: *: Catha edulis of the plant family Celastraceae is a mild stimulant plant known as Khat in Ethiopia. In Ethiopia, the history of Khat dates back to the 13th century, and communities produce and/or consume Khat leaves for social, religious, cultural and economic purposes. This study aimed to assess the association between Khat production and consumption on food security and dietary diversity among rural households in Ethiopia.*

Method*: A panel survey using quantitative methods was conducted in two regions of Ethiopia. Using an open Data Kit (ODK) a panel survey was conducted and analyzed applying a multivariable linear regression model.*

Result*: The likelihood of food insecurity was twice as high among non-Khat consumers and Khat producers compared to households who neither produce nor consume Khat, (AOR: 2.17 [95%CI: 1.25, 3.76], p<0.1. On average, households that produced and consumed Khat were 1.5 times more likely to have high dietary diversity (AOR: 1.51 [95%CI: 1.09, 2.08], p<0.01).*

Conclusion*: Although Khat is an important source of income for farmers throughout the year, our findings highlighted that Khat production and non-consumption were negatively associated with food security. The possible pathways of this association could be through the household subsistence farming and cash crop (Khat) interaction. Food security interventions should consider Khat production and consumption practices among households in Khat-producing and consuming areas of Ethiopia.*

Keywords*: Khat chewing; food security; Dietary diversity; QTR + EPI-2.*

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Introduction

Khat (*Catha edulis*): a stimulant plant which belongs to the plant family Celastraceae was named by the naturalist Peter Forsskål (1732–1767) [1]. It is also named as Abyssinian tea, Miraa, and African salad [2,3,9]. Leaves, buds and soft stems are chewed for social and cultural purposes such as ceremonial, recreational, traditional medicine, to boost energy and prevent hunger [4,5]. The legality of Khat has been questioned and internationally it is not listed as a controlled substance [7, 10,11].

Hundred grams of fresh leaves contain 36 mg cathinone and 120 mg cathine, which have appetite suppressing effect [6,13]. A recent study by Girma *et al.* reported that Khat users are physically small and have a decreased Fat Mass and Body Mass Index, which is related to a decrease in food intake [17]. In vivo trials on rats have shown that it decreased food intake and increased locomotor activity [12,15,16]. Khat consumption causes constipation, tachycardia, palpitation, increased blood pressure, anorexia, stomatitis, esophagitis, gastritis, periodontitis and oral leucoplakia [15,18.19].

In Ethiopia, Khat production and consumption are integrated into the culture, economy and livelihoods of rural households. Its farming, consumption and trading has evolved from traditional contexts into new, urban and commercial environments. The economic value in contrast with its damaging effect on health and society has led to divergent perspectives on its use. Some condemn Khat consumption as a health hazard, drains household budget, and reduces local food production [14, 22, 23].

Others found that Khat can be cultivated in small and low moisture plots with minimal investment, and it is frequently harvested to purchase food crop [8, 30]. Farmers' decision to plant Khat is also a result of its endless demand and growing market [20, 24, 36]. In 2014-2015, more than three million farmers cultivated Khat in Ethiopia [25, 26]. Khat production makes economic sense in areas where population growth has led

to a decrease in the average farm size and where households are unable to support themselves through subsistence crops or lower priced cash crops. It also provides wealth for leaf wholesalers, retailers, agents and farmers [27,29, 32].

Growing and chewing Khat could affect household food security and food diversity, potentially by displacing staple crops and, as a cash crop, reducing women's entitlement to food. Poor health and working culture are also additional pathways compromising household livelihood [33, 34, 35].

Khat generates revenue for Ethiopia. According to the 2003/04 Ethiopian economic survey, earnings from Khat exports, which were 272.4 million Birr (USD 38 million) in 1997/98, rose to 758.9 million Birr (USD 89 million)[31]. The 2012/13-2014/15 Commercial Bank of Ethiopia annual export reports that Khat contributed USD 272.4 million, accounting for 9 percent of the total export earnings in the review period [37].

Khat chewers spend a substantial amount of their time and earnings on Khat and are often irritable and away from home, which could lead to family disintegration [20,21].Whether Khat cultivation affects farmers' quality of life, e.g., by providing food security and improving living standards as a long-term coping strategy, or whether it has social, psychological, physical and economic consequences, leading to poverty, unemployment and illness, is a broad research topic that should be further explored.

As the current findings are more anecdotal, ambivalent, and affected by confounding factors, more studies are needed to improve the evidence base. This study aimed to determine the association of Khat production and/or consumption with household food security and dietary diversity in rural Ethiopia.

Methods and materials

This study was conducted within two regions of Ethiopia (Oromia and the Southern Nation, Nationality and People's). Expanded Program on Immunization (QTR + EPI-2) method was used to choose Subsequent households until the sample size (1200 households) reached. Data were collected using pre-tested, interviewer-administered questionnaires with Samsung tablets using Open Data Kit (ODK). Data were regularly transferred to a server every week by wireless cellular technology.

Measurements

Khat consumer: A person who consumed Khat habitually (a minimum of once a week) in bundles (one bundle=up to 500 g of edible leaf).

Khat producer: A person who had Khat plants in the farm or backyard on minimum of 0.002 hectares.

Households Khat production and consumption status was grouped into four categories -independent variables. Khat no producer and no consumer: A household that neither produced nor consumed Khat.

Khat Producer consumer: A household that produced and consumed Khat. Khat Producer no consumer: A household that produced but did not consume Khat.

Khat no producer consumer: A household that did not produce but consumed Khat.

Confounding variables: non-food household expenditures, land size for crop production, crop variety, household size and non-agricultural income type were measured.

Household food insecurity and the Dietary Diversity Score (DDS) were considered dependent variables. DDS (HDDS) was calculated considering the number of 12 food groups consumed in the previous 24 hours, and foods were grouped into tertiles, and the highest tertile was used as the highest HDD group, while the first and second tertiles were considered the lowest HDD group [38]. Household food insecurity was measured using the household food insecurity Access Scale (HFIAS) in the past 30 days which has been validated for use in developing countries [39, 40].

Data quality

The questionnaire was pre-tested with 5% of the total sample that was not included in the actual study. A 12-day intensive training was provided to the data collectors and supervisors. The data manager reviewed the data submitted from the field on a weekly basis.

Statistical analyses

Data were exported to STATA version SE 12(Stata Corp LP, College Station, Texas, USA), and were cleaned and checked for missing values and outliers before the analyses. Bivariate analysis was performed, and the means and proportions were compared using T -tests, ANOVA and Chi-square tests after checking all assumptions. Khat production and consumption was included as the main predictor variable in both models. Multivariable linear regression was applied with HDDS and household food insecurity as a response variable. The results were presented as adjusted odds ratios (AORs) and 95% confidence intervals (CIs). All tests were two-sided, and p values <0.05 were considered statistically significant.

Ethical consideration

Ethical approval was obtained from Jimma University institutional review board. Written permission was obtained from each responsible body, and informed verbal consent was obtained from study participants. Personal identifying information was not included in the questionnaire.

Results

Of the 1200 households included in the study, complete data were available for 1169 (response rate of 97.4%). A significantly higher proportion of Khat consumers, 379 (66.7%), were also producers ($p<0.001$).

As presented in Table 1, HDDS differed between the categories of Khat production and consumption, by the groups of non-food item expenditures and between those with a lower vs. higher mean land size

(p<0.0001). Similarly, there was a difference between those with a lower mean household size and those with a higher mean household size (p<0.0001).

Table 1: Association between Khat Production-Consumption and Household Dietary Diversity Score

Dietary diversity score(DDS) **Predictors**	High*(n/%)	Low (n/%)	Chi (p) value
Khat production-consumption			
No Khat consumer and no Khat producer	99(20.41)	386(79.59)	19.54(<0.001)
Khat consumer and Khat producer	119(32.16)	251(67.84)	
Khat consumer and no Khat producer	43(23.24)	142(76.76)	
No Khat consumer and Khat producer	21(17.50)	99(82.50)	
Non food household expenditures			
<3 types	20(11.63)	152(88.37)	34.95(<0.001)
3-5 types	192(23.82)	614(76.18)	
>5 types	70(38.46)	112(61.54)	
Crop variety			
Mono-cropping	64(18.93)	274(81.07)	7.49(0.006)
>=2crops	218(26.52)	604(73.48)	
Nonagricultural income			
No	164(24.40)	508(75.60)	0.0077(0.930)
Yes	118(24.18)	370(75.82)	
Household size (mean±SD)	6.09(±2.07)	5.82(±2.13)	-1.88(0.03)
Land area used for crop production (mean±SD)	0.68(±1.16)	0.38(±1.10)	-3.29(0.001)

As presented in Table 2, the multivariable logistic regression showed that on average, Khat consumers and producers were 1.5 times more likely to have high dietary diversity (AOR: 1.51[95%CI: 1.09, 2.08], p<0.01) than no consumer no producers. Similarly, households with 3-5 nonfood household expenditures were two times more likely to have high dietary diversity (AOR: 2.20[95%CI: 1.33, 3.62], p<0.002), and households with 6 and more non-food household items were four times more likely to have high dietary diversity (AOR: 4.06 [95%CI: 2.31, 7.16], p<0.001).

Table 2: Multivariable Logistic Regression Model Predicting the Effects of Khat Production and Consumption on Dietary Diversity Score.

DDS	AOR	Std. Err.	Z	95% CI.	P>p>z
Khat production and consumption					
No Khat consumer and no Khat producer	1.00				
Khat consumer and Khat producer	1.51	0.25	2.48	(1.09,2.08)	0.013
Khat consumer and no Khat producer	1.07	0.23	0.31	(0.70,1.62)	0.75
No Khat consumer and Khat producer	0.81	0.22	-0.78	(0.48,1.37)	0.43
Nonfood household expenditures					
Expenditure, <3 types	1.00				
Expenditure, 3-5 types	2.20	0.56	3.08	(1.33,3.62)	0.002
Expenditure, >=6 types	4.06	1.17	4.85	(2.31,7.16)	<0.001

Crop total					
Mono-cropping	1.00				
>=2 crops	1.06	0.20	0.29	(0.73,1.53)	0.77
Household size	1.03	0.04	0.77	(0.96,1.10)	0.44
Land area used for crop production (ln)	1.15	0.09	1.81	(0.99,1.33)	0.07
Con.	0.11	0.04	-6.46	(0.05,0.21)	<0.001

As illustrated in Fig 1 the different Khat producer and consumer groups differed significantly in food insecurity. The highest prevalence of food insecurity (83.3%) was observed among Khat producers and not consumers.

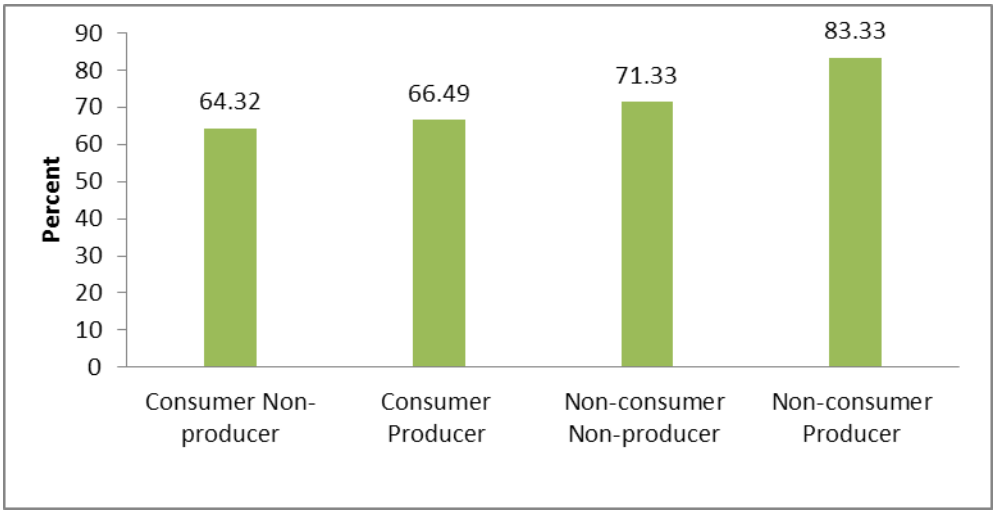

Fig 1. Proportion of Households with Food Insecurity by Khat Consumption and Production Status (p=0.001).

Khat production and consumption was associated with food insecurity (p=0.01). The prevalence of food insecurity decreased as the non-food household expenditure groups progressed from the lowest to highest (p<0.001). A decrease in food insecurity observed (p<0.001) when crop variety changed from mono-cropping to more than one crop type. Food insecure households had a significantly lower mean land size than those that were food secure (p=0.01). Likewise, food insecure households had a significantly higher mean household size than those that were food secure (p=0.001).The prevalence of food insecurity increased proportionally as non-agricultural income type increased.

As presented in Table 3, food security differed between the categories of Khat production and consumption, by the groups of non-food item expenditures and between those with a lower vs. higher mean land size (p<0.0001). Similarly, there was a difference between those with the group of mono cropping vs. more than one crop variety producers (p<0.0001).

Table 3. Association between Predictor Variables and Household Food Insecurity

Food Security

	Insecure (n %)	Secure (n/%)	Chi(p-value)
Khat production and consumption			
No Khat consumer and no Khat producer	346(71.34)	139(28.66)	15.56(0.01)
Khat consumer and Khat producer	246(66.49)	124(33.51)	
Khat consumer and no Khat producer	119(64.32)	66(35.68)	
No Khat consumer and Khat producer	100(83.33)	20(16.67)	
Nonfood household expenditures			
Expenditure, <3 types	150(87.21)	22(12.79)	30.64(<0.001)

Expenditure, 3-5 types	547(67.87)	259(32.13)	
Expenditure, >=6 types	114(62.64)	68(37.36)	
Non agricultural income type			
No non-agricultural income	448(66.67)	224(33.33)	8.01(0.005)
More than one non-agricultural income	363(74.39)	125(25.61)	
Crop variety production			
Mono-cropping	268(79.29)	70(20.71)	19.94(<0.001)
>One crop variety	543(66.06)	279(33.94)	
Household size (mean ±SD)	5.79(±2.11)	6.09(±2.14)	2.15(0.02)
Land area used for crop production (mean ±SD)	0.57(±1.06)	0.12(±1.10)	10.00(<0.001)

As shown in Table 4, the prevalence of food insecurity decreased by 31% among Khat consuming and non-producing households compared to non-consuming and non-producing households (AOR: 0.69[95%CI: 47, 1.01], p<0.5). In contrast, the likelihood of food insecurity was two times higher in households that produced but did not consume Khat than in households that neither produced nor consumed Khat (AOR: 2.17[95%CI: 1.25, 3.76], p<0.1). The likelihood of food insecurity decreased by 34% for each unit increase in land area used for crop production (AOR: 0.66[95%CI: 0.59, 0.74], p<0.001).

Additionally, the likelihood of food insecurity was 70% less among households with 3-5 types of nonfood household expenditures (AOR: 0.30[95%CI: 0.19, 0.50], p<0.001). Similarly, food insecurity was 71% less in households with ≥6 types of nonfood household expenditures compared with households with less types of nonfood household expenditures (AOR: 0.29[95% CI: 0.16, 0.52], p<0.001)

Table 4: Multivariable Logistic Regression Model Predicting the Likelihood of Household Food Insecurity in Rural Households of Ethiopia

Household food insecurity	AOR	[95% CI]	p-value
Khat production and consumption			
No Khat consumer and no Khat producer	Ref.		
Khat consumer and Khat producer	0.99	(0.72, 1.36)	0.94
Khat consumer and no Khat producer	0.69	(0.47, 1.01)	0.05
No Khat consumer and Khat producer	2.17	(1.25, 3.76)	0.01
Land area used for crop production	0.66	(0.59, 0.74)	<0.001
Nonfood household expenditures			
Expenditure, <3 types	Ref.		
Expenditure, 3-5 types	0.30	(0.19, 0.50)	<0.001
Expenditure, >=6 types	0.29	(0.16, 0.52)	<0.001
Nonagricultural income type			
No nonagricultural income	Ref.		
More than one non-agricultural income type	1.17	(0.88, 1.55)	0.29
Crop variety production			
Mono-cropping	Ref.		
>One crop variety	0.84	(0.60, 1.18)	0.32
Household size	1.02	(0.95, 1.09)	0.59

Discussion

This study indicated that, higher proportions of Khat consumers were Khat producers. The land area currently used for Khat plantation is 44% of that used for coffee cultivation [25]. From 2001/02 to 2014/15, the land for Khat farming increased by 160%, expanding throughout Ethiopia [31,41]. Findings from Khat growing areas have indicated that farmers intercrop Khat with subsistence crops such as vegetables, fruits and maize. Land that is not favored for other crops is also shifted to Khat plantation [26,42]. In addition, cash cropping has a possible positive `spillover effect` of providing credit, farming resources, and agricultural extension training and could potentially diversify dietary patterns [43]. By contrast, other studies have shown that chronic Khat consumption can drain family resources and that its production is intensifying at the expense of staple crops, with potential implications for food availability and consumption reduction [30,44]. However, the transformation of money from cash crops to other non-household food items and men`s control of cash crop incomes could leave women without the resources needed to feed their family [23,28,44].

This study found that households that produced and consumed Khat had greater dietary diversity than those that did not produce or consume; that could be due to its frequent harvesting in all seasons and is sold with high demand. An income from selling Khat could contribute to daily food crop purchase and consumption.

Although this study investigated the effects of Khat production and consumption on dietary diversity and food insecurity, alternative explanations such as land size for crop production, non-food household expenditures, non-agricultural income type, household size and crop diversity were addressed during the analysis. Non-agricultural income did not play a significant role in dietary diversity. This finding supports the hypothesis that farmers strategically use non-agricultural incomes to cope with the periods of poor agriculture returns or of inconsistent markets for their harvest [45,46]. Although collecting accurate income data is a challenging task, further research is needed to understand the factors that could improve and sustain household income and dietary diversity.

The results of this study indicated that farmers' household size did not play a significant role in dietary diversity for larger families. However, this finding is questionable, as it did not account for the role of human power or the proportions and composition of household members' age and gender. Studies recommend evaluating the association of household size with dietary diversity, food consumption and poverty in general with caution [47,48].

This study showed that compared to households that did not produce or consume Khat, household food security increased for consumers and non-producers but decreased for non-consumer–producers. The possible pathway for the effects of consuming and not producing Khat on food security during the lean season (data collection period) could involve the relatively low price of Khat due to the high production. However, this hypothesis should be confirmed with more evidence on the amount of Khat leaves consumed and how many family members are habituated. Not producing Khat could also suggest that land is used for crop production, while for households that do not consume but do produce Khat, food insecurity might increase due to farmers' tendency to produce or substitute their land for Khat plantation.

Food security is a multidimensional phenomenon. Crop production and sustainability, food availability and distribution (access), clean water, livelihood opportunities, education, off-farm income and access to health care are among the many predictors [49,50]. Food availability is a meaningful indicator of food security. The success of crop production depends on market access which is a better strategy for increasing food security than focusing on agricultural production alone [47].

This study indicated that in the presence of Khat production and consumption, non-agricultural income is not a pathway to food security and edible crop production from their small farm is highly valued for household livelihood. Evidence from Ethiopia and Uganda suggests that farm income accounts for more than 70% of total income. In most developing countries, subsistence agriculture in small farms contributes to food security though land and capital are scarce and the fixed land size with rural population growth is creating sub-divisions of small farms [41,51].

In Ethiopia, Khat consumption has expanded and has become a sociocultural and economic practice. Further follow-up research is needed to unpack the effect of substituting crop land for Khat. The findings of this study provoke debate whether small Ethiopian agriculture holdings should live with Khat or without it. Furthermore, questions remain regarding the outcomes of Khat production and whether Khat should be considered a controlled drug or a licit substance to be regulated.

Conclusion

This study identified that of the four household groups defined based on their Khat production and consumption, (a) Household food security was higher for consumers who were not producers but was lower for those who were neither consumers nor producers. (b) Khat producers and consumers had a more diverse diet than non-producers–non-consumers, which could be due to an increase in Khat productivity during the lean season, when income from Khat can increase and be used to purchase staple foods. Although Khat generates cash it may not have a positive effect on food security as the income from Khat can be used for other expenses. Livelihood and agricultural development interventions should consider Khat production and consumption effect among households in various Khat -producing areas of the country.

Conflict of interest
The author has no competing interests

Author contribution
BWA: Conceptualization, Methodology, Investigation, Formal analysis, Writing - review & editing.

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Original Article

The Relationship Between Kidney Function and Peripheral Artery Diseases in Patients with Metabolic Syndrome In a Resource Limited Setup: A Retrospective Record Review

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Abstract
***Background**: Metabolic syndrome (MetS) is characterized by a cluster of cardiovascular risk factors and has an impact on the prevalence of chronic kidney diseases (CKD). We aimed to investigate the association between CKD and peripheral arterial diseases (PAD) in MetS patients.*
***Patients and Methods**: This retrospective record review was performed among patients with and without MetS over seven months. MetS was defined according to NCEP ATPIII criteria, PAD was diagnosed by an ankle-brachial index (ABI) <0.9 and confirmed by angiography. Subjects were categorized on the basis of estimated Glomerular filtration rate (eGFR). The ANOVA test was applied to compare the three classes of eGFR. Boxplots were used to compare kidney biological parameters between males and females, MetS abnormalities and association of PAD with CKD.*
***Results**: From 342 patients, 56.40% were females, 77.8% with MetS, and 17.3% with PAD, 79.9% diabetics, 50.9% hypertensives, and 37.1% with dyslipidemia. The mean age was 61.56±17.30 years. Significant differences (p<0.05) were highlighted for age, anthropometric characteristics, diabetes, dyslipidemia, hypertension, PAD, family history and biochemical parameters. High levels of uric acid, albuminemia, micro-albuminuria and caliciumia in MetS patients were observed in both genders. These parameters increased with number of MetS components. CRP levels and lipid profile were significantly higher (p<0.05) in CKD patients. The prevalence of PAD in patients without CKD was 10.16% vs. 47.45 % in subjects with CKD.*
***Conclusion**: The coexistence of CKD and PAD was associated with MetS abnormalities and an inflammatory state, suggesting that the control of metabolic disorders may form part of the preventive measures for PAD and CKD.*

***Keywords**: CKD, Peripheral arterial disease, Metabolic syndrome, eGFR, Ankle-brachial index.*
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Introduction

Metabolic syndrome (MetS) is a cluster of various metabolic disorders including obesity (abdominal obesity), fasting or postprandial hyperglycaemia, hypertension and dyslipidaemia (high plasma triglycerides (TG) and low plasma high density lipoprotein cholesterol (HDL)). This clustering was first noted in 1923 by Kylin E (1). Subsequently, MetS was defined by several international bodies, including the WHO and EGIR (1999), Adult Treatment Panel III of the National Cholesterol Education Program (NCEP-ATPIII) (2001), AACE (2003), NCEP-R (2004), and IDF (2005) (2). The most widely accepted definition is that of the NCEP-ATPIII, which identifies MetS as the combination of at least three of the following five risk factors: abdominal obesity defined as a waist circumference ≥102 cm for men and ≥88 cm for women, high triglyceride (TG) levels ≥ 1. 5 g/L, low high-density lipoprotein (HDL) cholesterol (≤ 0.4 g/L for men and ≤ 0.5 g/L for women, blood pressure ≥ 130/85 mmHg, and fasting blood glucose ≥1 g/L (3).

Metabolic syndrome has become a common phe-

nomenon in several countries, where its prevalence has reached epidemic proportions, not only in the United States and the urbanized world, as well as in developing countries (4, 5). There is growing evidence of an association between kidney disease and MetS components (6). Several studies have confirmed this association, in which the number of MetS components has a positive impact on the prevalence of chronic kidney disease (CKD) (7-9). In fact, these abnormalities may be involved in the development and progression of reduced estimated glomerular filtration rate (eGFR). For example, arterial hypertension may be a major risk factor for the progression of renal dysfunction, or even CKD (10). Fatty tissue expansion and insulin resistance (IR) promote the chronic inflammation and oxidative stress that lead to renal failure. These factors may induce endothelial dysfunction, activation of the renin-angiotensin-aldosterone system and imbalance of adipokines. Inflammation and IR are the most common causes of microvascular and podocyte damage. These events lead to hypertension, albuminuria and parenchymal lesions. In addition, dyslipidaemia and excess nutrients too can affect mitochondrial function and promote the progression of renal cell damage (11).

Metabolic syndrome is characterized by a cluster of cardiovascular risk factors that are associated with a high risk of developing coronary heart disease, stroke, heart disease and peripheral arterial disease (PAD) (4, 11-13). Over the last decade, the prevalence of PAD has increased by 25% worldwide, reaching more than 200 million people worldwide (14, 15), prompting the Kidney Disease / Improving Global Outcomes (KDIGO) association to organize a conference in 2020 on the clinical controversies surrounding central disease and PAD in renal failure. The KDIGO reported that cardiovascular events account for the majority of deaths in people with CKD (16). However, the link between MetS, PAD and KD is not fully understood. Hence, our focus is to examine the association between CKD and PAD with MetS.

Patients and methods

Study design and area

A retrospective record review was conducted on individuals with and without MetS, who were admitted to the internal medicine unit of the "Ben Badis" public hospital and the Larbi Ben M'hidi Diabetes Centre in the Sidi-Bel-Abbes province in northwestern Algeria between between January 2019 and April 2022.

Data collection

During the 17-month study period, thorough medical records containing details of all hospitalized patients were reviewed to collect information on medical history (including diabetes, hypertension, dyslipidemia, and cardiovascular conditions) and a range of biochemical parameters (such as HbA1c, fasting glucose levels, HDL, LDL, total cholesterol (TC), triglycerides (TG), creatinine, urea, albumin levels, microalbuminuria, uric acid, calcemia, C-reactive protein, Na, K, chloride, and Cl). A total of 516 files were collected, excluding patients who met the exclusion criteria, leaving 315 files for this study.

Inclusion and Exclusion criteria

This study included adult men and women with and without MetS. Participants had to agree to take part in the interview and have a complete medical file.

Individuals suffering from cancer, autoimmune diseases, infectious diseases, HIV or HCV, pregnant women and patients with incomplete medical records were excluded.

Anthropometric measurements

Anthropometric measurements, including body weight (in kilograms), height (in meters), and waist circumference (in cm), were obtained using an electronic balance, a body meter and a tape measure, respectively.

The body mass index (BMI) was calculated as follows: BMI (Kg/m2) = weight (Kg) / height 2 (m2).

Blood pressure was measured using a manual handheld sphygmomanometer.

MetS, PAD and CKD definition

NCEP ATP III criteria were used to defined MetS, waist circumference ≥ 102 cm for men or ≥88 cm for women, triglycerides ≥1.5g/l, HDL <0.4g/l, for men or <0.5g/l for women, hypertension (systolic blood pressure ≥13cmHg or diastolic blood pressure ≥ 8.5 cmHg) and impaired glucose tolerance (fasting plasma glucose ≥1.1g/l) or diabetes (3). PAD was diagnosed by an ankle-brachial index (ABI) <0.9 and confirmed by angiography. Kidney function was categorized on the basis of eGFR >90, 60 to 89 and 15 to 59 ml/min per 1.73 m2 for non-kidney diseases (NKD), moderate kidney diseases (MKD), and chronic kidney diseases (CKD), respectively.

Calculation of eGFR

Estimated glomerular filtration rate was calculated according to Modification of Diet in Renal Disease study formula (MDRD) (17).

MDRD formula: eGFR =186.3 * (serum creatinine-1.154) * (age-0.203) *1.212 (if black) * 0.742 (if female).

Statistical analysis

Data were analysed using SPSS 20.0. Results are expressed as means ± standard deviations. The comparison of mean values and qualitative variables between group of patients without MetS (without MetS) and with MetS (with MetS) was performed using independent student's t test and Chi-square test, respectively. ANOVA test was applied to compare the three classes of eGFR. Box plots were used to compare kidney assessment between males and females, MetS abnormalities and association of PAD with CKD.

Ethical consideration

Ethical clearance was obtained from the Human Resources Sub-Management (HRSM) of Ben Badis in the Sidi-Bel-Abbes (Reference number: / 2021/م ف م ب .(1661

Results

The basic characteristics of the patients are shown in table 1. Following the exclusion and inclusion criteria, 315 participants were chosen from a pool of 516 files, 56.40% of whom were women and 43.6% men. Among the individuals included, 77.8% were diagnosed with MeS and 17.3% with PAD. The overall of mean age was 61.56 ± 17.30 years (51.80± 22.13 in patients without MetS and 64.35± 14.54 in patients with MetS), with a significant difference (p<0.001) between the two groups. Our results revealed that 79.9% of patients were diabetics, 50.9% were hypertensives and 37.1% were with dyslipidaemia.

Comparing patients with MetS to those without MetS,

Table 1: Baseline characteristics of the Study population according to presence or absence of Metabolic Syndrome at Ben Badis" public hospital from January 2019 to April 2022

Parameters	Total	Without MetS	With MetS	p value
n (%)	342	76 (22.20)	266 (77.80)	
Age (years)	61.56±17.30	51.80±22.13	64.35±14.54	<0.001*
Patient's systolic pressure (cmHg); Mean ±S.D	12.51±2.35	11.28±1.84	12.85±2.37	0.070*
Patient's diastolic pressure(cmHg); Mean ±S.D	6.9±1.43	6.7±1.35	7.04±1.42	0.586*
HbA1c (%); Mean ±SD	8.66±2.12	7.65±2.16	8.20±2.09	0.803*
Fasting glycaemia (g/l); Mean ±S.D	1.56±0.71	1.56±0.76	1.56±0.69	0.298*
HDLc (g/l); Mean ±S.D	0.44±0.14	0.50±0.11	0.42±0.14	0.209*
LDLc (g/l); Mean ±S.D	0.98±0.47	1.07±0.31	1.11±0.39	<0.001*
TC (g/l); Mean ±S.D	1.71±0.48	1.63±0.36	1.73±0.51	0.009*
TG (g/l); Mean ±S.D	1.38±0.70	1.04±0.45	1.48±0.73	<0.001*
Creatinine (g/l); Mean ±S.D	14.57±10.42	12.62±8.22	15.14±10.92	0.007*
Urea (g/l); Mean ±S.D	0.71±0.71	0.51±0.40	0.77±0.76	0.007*
Albuminemia (g/dl); Mean ±S.D	39.05±24.8	31.24±18.76	41.26±25.87	0.017*
Micro-Albuminuria (g/24h); Mean ±S.D	2.27±12.88	51.69±34.34	91.00±78.46	<0.001*
Uric acid (g/l); Mean ±S.D	58.28±23.79	40.97±17.82	63.22±22.97	0.023*
eGFR (mL/min/1.73m^2); Mean ±S.D	62.73±38.29	71.57± 40.22	60.17±37.40	0.267*
Calcemia; Mean ±S.D	77.90±20.49	69.49±21.92	80.30±19.45	0.032*
CRP (g/l); Mean ±S.D	42.70±41.37	45.51±45.26	42.01±40.41	0.048*
Na (g/l); Mean ±S.D	133.26±10.00	133.02±8.71	133.33±10.35	0.709*

K (g/l); Mean ±S.D				
	3.91±1.19	3.92±1.09	3.91±1.22	0.601*
Cl (g/l); Mean ±S.D				
	95.35±95.35	98.83± 9.02	94.26±16.18	0.037*
P (g/l); Mean ±S.D				
	48.96±33.090	46.11±22.03	49.58±35.06	0.093*
Patients' gender; n (%)				
Female	193 (56.4)	46 (13.5)	147 (43)	0.247#
Male	149 (43.6)	30 (8.8)	119 (34.8)	
Corpulence; n (%)				
Normal weight	90 (29)	39 (12.6)	51 (16.5)	<0.001#
Overweight	125 (40.3)	19 (6.1)	106 (34.2)	
Obese	95 (30.6)	7 (2.3)	88 (28.4)	
Diabetes; n (%)				
No	59 (20.1)	24 (8.2)	35 (11.9)	<0.001#
Yes	235 (79.9)	28 (9.5)	207 (70.4)	
Dyslipidaemia; n (%)				
No	215 (62.9)	71 (20.8)	144 (42.1)	<0.001#
Yes	127 (37.1)	5 (1.5)	122 (35.7)	
Hypertension; n (%)				
No	168 (49.1)	66 (19.3)	102 (29.8)	<0.001#
Yes	174 (50.9)	10 (2.9)	164 (48)	
PAD; n (%)				
No	283 (82.7)	70 (20.5)	213 (62.3)	0.008#
Yes	59 (17.3)	6 (1.8)	53 (15.5)	
Family history (CVD, Hypertension, Diabetes, Dyslipidaemia); n (%)				
No	64 (58.1)	26 (38.2)	38 (19.9)	0.003#
Yes		42 (61.8)	153 (80.1)	
Waist circumference classes				
Normal	92 (27.8)	45 (13.6)	47 (14.2)	<0.001#
Obese	239 (72.2)	25 (7.6)	214 (64)	

(*) p value for student t test; (#) p value for Chi-square test; p ≤ 0.05 was considered as statistically significant. MetS: metabolic syndrome, HbA1c: glycated haemoglobin, HDLc: high-density lipoproteins, LDLc: low-density lipoprotein, TC: total cholesterol, TG: triglyceride, eGFR: estimated glomerular filtration rate, CRP: C-reactive protein, PAD: peripheral arterial diseases, CVD: cardio-vascular diseases.

Our finding about the comparison of renal parameters between patients with and without MetS highlighted high levels of uric acid, albuminemia, micro-albuminuria and calicaemia in MetS patients, similar values were emphasized in male and female gender (figure 1). Figure two shows comparison of renal parameters (urea, creatinine, uric acid, albuminemia, micro-albuminuria and calcaemia) according to number of MetS abnormalities, our finding revealed that levels of al most of these parameters increased with number of MetS abnormalities.

Comparison between the three eGFR classes through ANOVA test reveals significant differences ($p<0.05$) in CRP levels and lipid profile (HDL, LDL, TC, TG) with higher values in patients of the first class.

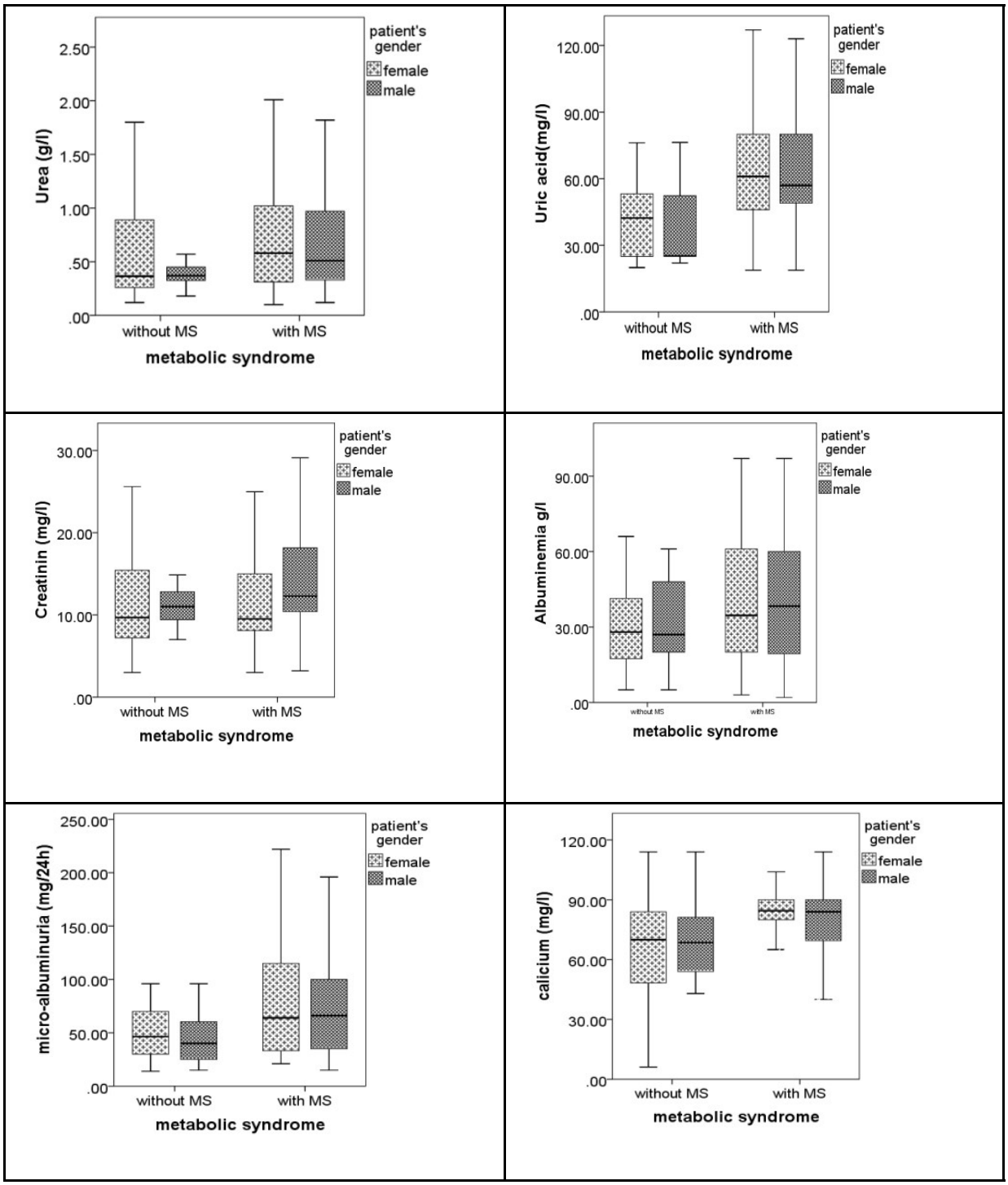


Figure 1: comparison of kidney assessment between males and females according to the metabolic syndrome profile at Ben Badis" public hospital from January 2019 to April 2022

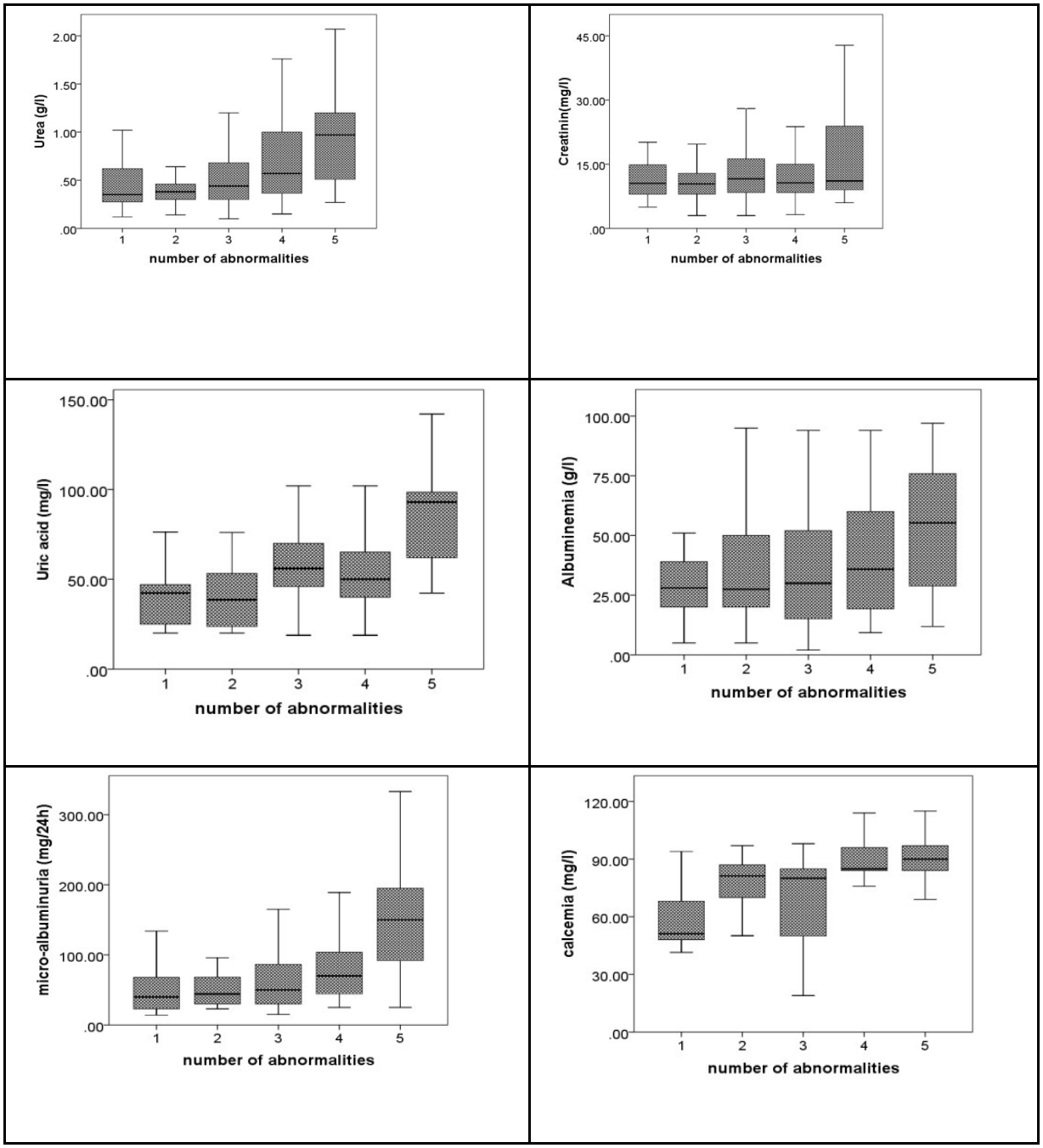


Figure 2: comparison of kidney assessment between metabolic syndrome classes at Ben Badis" public hospital from January 2019 to April 2022

No significant differences ($p>0.05$) were observed in age, urea, uric acid, micro-albuminuria, fasting glycaemia, HbA1c levels, BMI, systolic and diastolic pressure.

The group of patients with eGFR between 15 and 59 mL/min/1.73 m2 had higher percentage of diabetes, dyslipidaemia, hypertension, PAD and MetS compared to other groups, with a significant value ($p<0.05$) for hypertension and MetS (Table 2).

Table 2: Comparison of renal parameters, CRP and metabolic syndrome components between eGFR classes.at Ben Badis" public hospital from January 2019 to April 2022

Parameters	15< eGFR≤ 59 121(45%) CKD	60<eGFR≤89 101 (37.5 %) MKD	eGFR≥ 90 47(17.5%) NKD	P value*
Age(year)	68.60 ± 13.93	59.5 ± 11.03	63 ± 19.53	0.068*
Urea (g/l); Mean ±S.D	0.71 ± 0.45	0.47 ± 0.27	0.98 ± 1.43	0.160*
Uric acid(g/l); Mean ±S.D	64.24 ± 23.94	61.62 ± 22.5	55.91 ± 16.87	0.709*
Micro-Albuminuria (g/24h); Mean ±S.D	102.19 ± 82.35	74.24 ± 52.53	49.22 ± 33.7	0.147*
CRP (g/l); Mean ±S.D	54.14 ± 34.64	59.88 ± 25.74	23.10 ± 24.90	0.041*
Fasting glycaemia (g/l); Mean ±S.D	1.45 ± 0.56	1.63 ± 0.74	1.58 ± 0.42	0.608*
HbA1c (%); Mean ±SD	7.70 ± 2.22	8.6 ± 2.56	9.46 ± 2.31	0.174*
HDLc(g/l); Mean ±SD	0.37 ± 0.12	0.37 ± 0.10	0.61 ± 0.09	$<10^{-3}$*
LDLc(g/l); Mean ±SD	1.36 ± 0.56	1.27 ± 0.64	0.38 ± 0.24	0.002*
TC(g/l); Mean ±SD	2.20 ± 0.62	2 ± 0.56	1.30 ± 0.35	0.004*
TG(g/l); Mean ±SD	2.38 ± 0.79	1.86 ± 0.56	1.55 ± 0.58	0.007*
BMI (kg/m²)	29.39 ± 6.39	29.52 ± 4.07	26.80 ± 3.09	0.523*
Patient's systolic pressure (cmHg); Mean ±S.D	12.68 ± 2.10	13.68 ± 3.41	12.83 ± 1.16	0.410*
Patient's diastolic pressure(cmHg); Mean ±S.D	7.08 ± 1.45	7.59 ± 2.07	7.16 ± 1.16	0.580*
Diabetes; n (%)	93 (44.07%)	81(38.38%)	37 (17.53%)	0.833#
Dyslipidaemia; n (%)	57 (48.71%)	45 (38.46%)	15 (12.82%)	0.138#
Hypertension; n (%)	88 (56.05%)	53(33.57%)	16 (10.19%)	$<10^{-3}$#
MetS; n (%)	121 (45%)	101(37.5%)	47(17.5%)	0.014#
PAD; n (%)	28 (47.45%)	22(37.28%)	6(10.16%)	0.255#

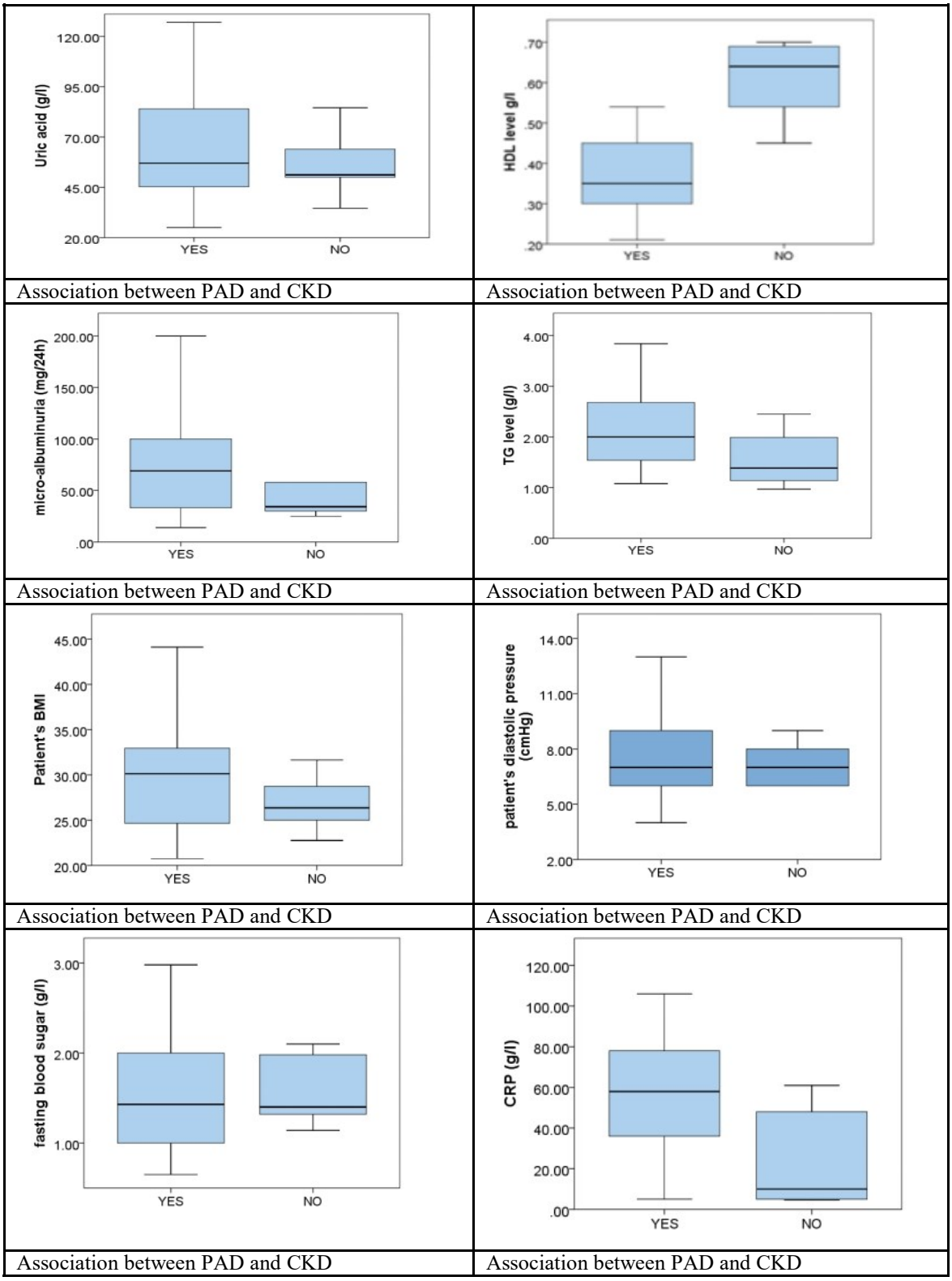
(*) Comparison between eGFR classes using ANOVA test, (#) p value for Chi-square test; p ≤ 0.05was considered as statistically significant. eGFR: estimated glomerular filtration rate; CRP: C-reactive protein; HbA1c: glycated haemoglobin, HDLc: high-density lipoproteins; LDLc: low-density lipoprotein; TC: total cholesterol; TG: triglyceride; BMI: body mass index; MetS: metabolic syndrome; PAD: peripheral arterial diseases. The eGFR unit is expressed as: ml/min per 1.73 m2, NKD: non-kidney diseases, MKD: moderate kidney diseases, CKD: chronic kidney diseases.

The prevalence of PAD in patients without kidney diseases was 10.16% vs. 47.45 % in subjects with CKD (Table 2). The uric acid, micro-albuminuria, CRP, TG levels and BMI were elevated in the group of patients with PAD associated with CKD. However, HDL levels were higher in second group. Fasting glycaemia and diastolic pressure were nearly equal in both groups. The coexistence of KD and PAD was associated with MetS abnormalities and an inflammatory state (elevated CRP) (Figure 3).

Discussion

In the present study, we set out to investigate the complex interconnection between PAD and CKD with presence of MetS. A cross-sectional and longitudinal study involving a nationwide population in Taiwan pointed that having five abnormalities was associated with a more than twofold increase in odds of Kidney stone (KS) and all components of the MetS were associated with a higher prevalence of KS (18). A study of 3872 Korean men without KS underscored an elevated risk of KS in individuals with MetS at 1.77 times higher (1.157-2.711) (19). In 2004, Chen et al. reported that MetS was an independent risk factor of CKD (20). The Finding by Chang, et al demonstrated a strong association between MetS and KS (18), these findings were confirmed in recent studies (9, 21).

In our study population of adults with a mean age of 61.56 years, the prevalence of MetS was 77.80%, with women accounting for 56.4% of participants.



Association between PAD and CKD	Association between PAD and CKD
Association between PAD and CKD	Association between PAD and CKD
Association between PAD and CKD	Association between PAD and CKD
Association between PAD and CKD	Association between PAD and CKD

Figure 3: comparison of renal parameters, CRP and metabolic syndrome components according to association of peripheral arterial diseases with kidney diseases *at Ben Badis" public hospital from January 2019 to April 2022*

Our estimate was comparable to that reported in a cross-sectional and longitudinal cohort study of 121,579 participants registered at the Taiwan Biobank (mean ages were 54 ± 10 and 49 ± 11 years in the MetS and non-MetS groups, respectively, comprised 64% of the population, and 67% were affected by MetS), on the other hand, our figures were higher than those reported in a national cross-sectional study of 97,098 Chinese adults aged 18 years or older in 2010, in which the prevalence of MetS was 33.9% (31.0% in men and 36.8% in women) (18, 22). Our MetS participants had higher risk of CKD (45% of MetS patients had CKD and 37.5% had MKD) compared to those without MetS. Moreover, they had high BMI, blood pressure, HbA1c, LDL, CT, TG, serum creatinine, urea, serum albumin, Micro-Albuminuria, uric acid, serum calcium and serum phosphor levels and low eGFR, HDL-C and CRP levels. Similar results were reported by Wu N et al. (23), participants with MetS were 1.82 times as likely to develop CKD compared to those without MetS (OR: 1.82, 95% CI: 1.19–2.78). In which the risk of CKD increased with the number of MetS components ($p < 0.001$). ORs for CKD were 1.25 (95% CI: 0.74–2.11), 1.95 (95% CI: 1.11–3.43), 2.29 (95% CI: 1.20–4.39), 4.28 (95% CI: 1.98– 9.25), and 4.93 (95% CI: 1.87–13.03) for one, two, three, four, and five MetS components versus zero (23). Our finding revealed elevated levels of uric acid, albuminemia, microalbuminuria and calcaemia in patients with MetS compared to those without MetS (figure 1). Similar values were underlined in males and females. Levels of all most of renal assessment parameters increased with number of MetS abnormalities.

It is well-known that diabetes and hypertension represent the most common drivers of reduced kidney function in the general population. Moreover, it is known that high triglyceride levels and low HDL-cholesterol levels are associated with an increased risk of CVD and may contribute to kidney dysfunction through their pro-inflammatory and atherogenic effects or by acting as a marker for insulin resistance in kidney diseases (24, 25). Two previous studies likewise outline an enhanced risk of KS in hypertensive patients. Furthermore, familial hypertensive patients tend to have hypercalciuria and hyperuricosuria, leading to KS (26-29).

Several epidemiological studies have established a link between low HDL levels and poor renal function or progression to CKD (30, 31). Interestingly, our results showed a high proportion of diabetes, dyslipidaemia, hypertension, PAD and MetS in patients with eGFR between 15 and 59 ml/min/1.73. Indeed, subjects in this eGFR class had high levels of LDL, TG and TC. Bowe et al estimated that patients with HDL-C concentrations below 30 mg/dL had a 10-20% higher risk of CKD than individuals with concentrations above 40 mg/dL (32). Our results likewise highlight the reduced levels of HDL in the group of people with chronic kidney disease.

The prevalence of PAD has increased over the last decade by more than 25% from about 160 million to over 200 million, particularly in low-income countries (15). Numerous studies have revealed a close correlation between PAD and components of MetS, as well as between lipid profile disorders and PAD in patients with MetS. In addition, CKD is now recognized as a significant independent risk factor for PAD (4, 33). Foley et al. In study of 1,091,201 subjects pointed out that, the prevalence of PAD was threefold higher in patients with CKD (35% in CKD patient vs. 9.6% in patient without CKD) (34). Abu et al. (35) established an association between age, duration of CKD, length of time on dialysis, PAD and cardiovascular risk. Consistent with these previous studies, we found that 47.45% of patients with CKD developed PAD compared to only 10.16% of patients without CKD. We found that uric acid, microalbuminuria, CRP, TG levels and BMI were elevated when CKD and PAD coexisted. However, HDL levels were lower. The association of CKD and PAD was linked to MetS abnormalities and an inflammatory state (high CRP).

Our investigation faced some problems that must be indicated. First, the sample size was limited since the cases were collected in a short period. Second, the generalization of our results to other populations may be limited because the prevalence of components of the MetS varies across population. Fourth, most patients already under antihypertensor, statins and oral antidiabetic drug these treatments may improve renal function, lower the risk of vascular events and improve the survival of PAD (36, 37). Whereas those with incomplete medical records were excluded.

Conclusion

High levels of LDL, TC, TG, and low HDL levels were associated with an eGFR between 15 and 59 mL/min/1.73 m2. Diabetes, dyslipidaemia, hypertension, obesity (components of MetS) and PAD were closely linked with kidney dysfunction. The coexistence of CKD and PAD was associated with MetS abnormalities and an inflammatory state (elevated CRP levels). We conclude that MetS can be considered as a potential risk factor for CKD and PAD, suggesting that correction of metabolic disorders could be part of preventive measures against the recurrence of CKD and PAD.

Conflict of interest

The authors declare that they have no known competing interests.

Funding

We have not received any fund for this study.

Data availability

Data can be shared up on reasonable request

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Original Article

Demographic and Clinical Characteristics of Deceased COVID-19 Patients in Oromia Region, Ethiopia: A Retrospective Record Review

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Abstract
***Background**: The mortality due to COVID-19 in low-income settings has been grossly underestimated. The gap in the estimated deaths as the cause of COVID-19 and observed deaths in Africa requires further investigation. Hence, we aimed to assess the socio-demographic characteristics, clinical and laboratory profiles of patients who died from COVID-19 at the treatment centers in the Oromia region, Ethiopia.*
***Method**: A retrospective chart review was conducted from all health facilities that reported more than ten COVID-19 deaths from April 2020 to November 2021 in Oromia. CSPro Data Entry and STATA version 14 were used for data entry and analysis, respectively.*
***Result**: Of the 594 COVID-19 deaths reported during the study period, 454 (76.4%) were captured in nine health facilities. Of the 454 participants, 288 (63.4%) were men and 192 (42.3%) were over 60 years. Cough and shortness of breath were the most prevalent symptoms. Cough and shortness of breath were the most prevalent symptoms. Upon presentation, 394 (97.28%) exhibited tachypnea, 78 (27.56%) had a fever, and 366 (84.92%) had oxygen saturation levels below 92%. At least one comorbidity was present in 60% of the individuals. The median length of stay in the facility before death was five days (IQR 2–8). Common laboratory tests include complete blood counts, renal function and liver function tests. In 35(15%) of cases, the estimated glomerular filtration rate was <30 ml/min/1.73 m2. Neutrophilia was in 83.9% of cases, lymphocytosis in 2.6% and elevated creatinine in 35%. Chest X-ray was the frequently used imaging modality with opacity was the most common finding. Antibiotics and steroids were administered primarily.*
***Conclusion**: Most of the cases had comorbidity and were older aged. However, a quarter of patients were less than 45 years and two-fifths of patients had no known comorbidity. Strengthening vaccine acceptance across all age groups has paramount importance in preventing the severity of disease and death.*

***Keywords**: COVID-19, SARS-CoV-2, Mortality, Pandemic, Oromia, Ethiopia.*
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Introduction

The coronavirus disease (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), caused significant mortality and huge socioeconomic consequences [1-3]. As of November 2, 2023, data, there were a total of 771 million confirmed COVID-19 cases reported to WHO, and about 6.9 million lives were lost [4]. The virus continues to spread with emerging potential variants for high transmission, increased virulence, and resistance to available vaccines [5]. In 2021, Africa experienced the highest SARS-CoV-2 infection rate, which has escalated rapidly. Yet the reported deaths remained low despite alarming predictions [6]. As of November 2, 2023, data shows 9.5 million confirmed cases have

been reported from Africa [4]. Ethiopia was ranked sixth in Africa, with 501,060 reported cases and 7,574 deaths as of November 3, 2023, data [7]. The true extent could be higher if regular and wide testing coverage existed in all parts of the country. Ethiopia has vaccinated a total of 68,856,793 people as of November 3, 2023 [4]. The presentations of COVID-19 diseases vary from mild symptoms of fatigue, myalgia, cough, sore throat, runny nose, sneezing, headache [8-10] to severe conditions like shortness of breath, hypoxia (SpO2< 92%) and systemic inflammations which need hospitalization [11, 12]. Severe COVID-19 disease may lead to critical and fatal conditions like acute respiratory distress, shock, myocardial injury, heart failure, coagulation dysfunction, and acute kidney injury [9-11]. Factors such as being over 60 years old, having comorbid conditions like chronic cardiac, renal, or pulmonary diseases, diabetes mellitus, or being infected with the human immunodeficiency virus are associated with increased severity [8, 9, 13, 14]. Populations may diverge in the demographic, clinical presentation, and laboratory findings of patients who die of COVID-19. Though there is plenty of published literature on COVID-19 deaths from different parts of the world, reports from Ethiopia are few and of a small sample size [13-15]. We, therefore, assessed the demographic and clinical characteristics of deceased COVID-19 patients in the COVID 19 treatment centers of Oromia region, Ethiopia.

Material and methods

Study setting and study population

Oromia is the most populous region with the largest geographical coverage in the country, with a regional projection estimated to be 44 million in 2015 Ethiopian fiscal year (EFY). There are 109 functional hospitals, 1,411 health centers, and 7,099 health posts according to the 2013 (EFY) health and health-related indicators published by the Ministry of Health [16].

An institution-based retrospective chart review was applied in this study. Medical records that had COVID-19 admission data were included. We included all health facilities in the Oromia region that reported more than 10 COVID-19-related deaths from April 2020 to November 2021. There were 7652 cases admitted to all health facilities in the region as of November 9, 2021. The mortalities were reported from one health center, four primary hospitals, one general hospital, and three teaching hospitals.

Data collection

The collected data include demographic information, cigarette smoking, comorbidities, length of hospital stay, symptoms upon presentation, vital signs, respiratory support type, laboratory results, imaging findings, and treatment modalities. Death from COVID-19 was defined as a death happening while patients were in a COVID-19 treatment center. The electronic data collection tool was developed and tested on ten randomly selected records, and appropriate revisions were made. Cis-Pro data entry application was employed. The data collectors were fourteen general practitioners involved in COVID-19 care at the selected health facilities. All were trained on the data collection tool and procedure.

Data analysis

The data were cleaned and analyzed using STATA version 14 (StataCorp. 2015. Stata 14 Base Reference Manual. College Station, TX: Stata Press). The categorical variables were summarized by percentage, and continuous variables were described using mean, median, and range.

Ethical consideration

Ethical approval (Ref. No: BEFO/HBTFH/1-16/1123, dated July 5, 2021) was obtained from the Oromia Health Bureau internal review board, and we sought permission from all health facilities. Data were collected anonymized with a unique identifier generated by the Cis-pro application. The confidentiality of the collected data was maintained throughout the study.

Results

Demographic characteristics and comorbidities

A total of 594 deaths due to COVID-19 were reported from health facilities in Oromia region, Ethiopia, in the period from April 25 2020 to November 9 2021. Of these deaths, 454 were confirmed COVID-19 deaths occurred in the nine selected health facilities for this study. Adama Hospital Medical College and Jimma University Hospital had the highest deaths, with 134(29.6%) and 92(20.3%), respectively.

The age range of those who died was from 4 months to 102 years, with a median age of 60 years (IQR 46 – 74). The majority of deaths were males, accounting for 288 (63.4%), and individuals over the age of 60, accounting for 192 (42.3%) (Table 1). Less than 1% of the deceased had a history of smoking cigarettes, and all smokers were male. More than half of the total deaths, 271 (59.7%), had at least one comorbidity, with hypertension being the most prevalent at 117 (25.8%). The median duration of stay in the facility before death was five days, with an interquartile range of 2 to 8 days.

Presenting clinical characteristics and vital signs

Upon arrival at the treatment centers, the prevalent symptoms were cough, observed in 427 (94%), and shortness of breath in 417 (94%). Approximately six out of ten individuals had a history of fever at presentation. In this study, vital signs were recorded for more than 80% of the patients, but temperature was the least recorded, being documented for only 62% of patients in this study. Upon presentation to the health facility, 78(27.6%) patients were febrile (>37.20C), and 394 (97.3%) were tachypneic (respiratory rate of > 21 breaths per minute). Additionally, 366 (84.9%) patients had oxygen saturation <92% on their first day of admission, and almost all of them required respiratory support (Table 3).

At the time of presentation, only four patients (0.9%) had mild COVID-19, 11 (2.4%) had moderate and 257

(56.6) had severe COVID-19 infection.
Out of 415 patients on their second day of admission, complete records were only available for 273, representing 66% of the total.

Table 1. Characteristics of patients who died of COVID-19 in Oromia region, Ethiopia from April 2020 to November 2021

Variables (N=454)	Categories	n (%)
Sex	Male	288 (63.4)
	Female	166 (36.6)
Age (years)	<18	7 (1.5)
	18-30	29 (6.4)
	31-45	77 (17.0)
	46-60	149 (32.8)
	61-102	192 (42.3)
History of cigarette smoking	Yes	4 (0.9)
	No	450 (99.1)
Had any comorbidity	Yes	271 (59.7)
	No	183 (40.3)
Number of comorbidity	0	183 (40.3)
	1	179 (39.4)
	2	69 (15.2)
	3	19 (4.2)
	4	4 (0.9)
Types of comorbidities	Hypertension	117 (25.8)
	Diabetes Mellitus	81 (17.8)
	Cardiac Disease	55 (12.1)
	Chronic kidney disease	21 (4.6)
	Neurologic disease	19 (4.2)
	Asthma	14 (3.1)
	Chronic liver disease	5 (1.1)
Length of facility stay	< 24 hrs.	39 (8.6)
	1 - 2 days	105 (23.1)
	3 - 5 days	111 (24.5)
	6 - 8 days	90 (19.8)
	9 - 50 days	109 (24.0)

Table 2: Presenting clinical symptoms of patients who died of COVID-19 in Oromia region, Ethiopia from April 2020 to November 2021

Signs and symptoms (N=455)	n (%)
Cough	427 (93.8)
Shortness of breath	417 (91.9)
Easy fatigability	292 (64.3)
Fever	266 (58.6)
Poor appetite	207 (45.56)
Chest pain	136 (30.0)
Headache	118 (26.0)
Myalgia	71 (15.6)
Arthralgia	60 (13.2)
Chills	48 (10.6)
Nausea/ Vomiting	41 (9.0)
Rigor	39 (8.6)
Sore throat	29 (6.4)
Loss of smell and taste	17 (3.7)
Orthopnea, PND	11 (2.4)
Runny nose	6 (1.3)
* Other	62 (13.6)

* Delirium, leg swelling, epigastric pain, body swelling, diarrhea, loss of consciousness, night sweating, body weakness, decreased urine output, failure to communicate, palpitation, abnormal body movement, etc,

Table 3: First-day vital signs of patients who died of COVID-19 in Oromia region, Ethiopia from April 2020 to November 2021

Systolic blood pressure (mmHg) category (n=398)	
< 90 mmHg	28 (7%)
90 - 129 mmHg	212 (53.3%)
≥ 130 mmHg	158 (39.7%)
Diastolic blood pressure (mmHg) (n=398)	
<80 mmHg	286 (71.9%)
81-89 mmHg	40 (10.1%)
≥ 90 mmHg	72 (18.1%)
PR (beat per minute) (n=419)	
< 60	8 (1.9%)
60 – 100	191 (45.6%)
> 100	220 (52.5%)
RR (breath per minute) (n= 405)	
< 11	2 (0.5%)
12 - 20	9 (2.2%)
>21	394 (97.3%)
Temperature (^{o}C) (n= 283)	
< 36	12 (4.2%)
36 – 37.2	193 (68.2%)
> 37.2	78 (27.6%)
SpO_2 (n= 431)	
< 92	366 (84.9%)
≥ 92	65 (15.1%)
Random blood sugar (mg/dl)	n= 284 (62.6%)
< 140	135 (47.5%)
140 – 199	76 (26.8%)
> 200	73 (25.7%)

Imaging

Patients were investigated using various imaging modalities, with chest X-ray being the most common, used in 174(38.3%), followed by abdominal ultrasound in 52(11.5%) cases. Opacity and bilateral lung involvement were the most common findings on chest x-ray.

Laboratory results

Complete blood count, renal function test, and liver function test were the most commonly performed laboratory tests. Most of the patients, 230 (83.9%), had neutrophilia, whereas only 7 (2.6%) had lymphocytosis. Around 35% of patients had higher creatinine and an estimated glomerular filtration rate < 60 ml/ min/1.73m^2.

Medications

Antibiotics and steroids were the drugs most frequently prescribed (Table 4. Vancomycin and 3rd and 4th generation Cephalosporin were used most often among the antibiotics.

Table 4: List of commonly used drugs for patient management.

S.N	**Drug (N=454)**	**n**	**%**
1	Dexamethasone	349	77
2	Vancomycin	329	72
3	Cefatazidime	224	49
4	UFH	197	43
5	Ceftriaxone	136	30
6	Cemitedine	89	20
7	Cefepime	78	17
8	Azithromycin	76	17
9	Lasix	67	15
10	Tramadol	50	11

Table 5: Complete blood count, renal and liver function profiles of patients who died of COVID-19 in Oromia region, Ethiopia from April 2020 to November 2021

Laboratory test	N	Range	n (%)
WBC count (10^3/ µL)	280	< 4	9 (3.2)
		4 – 11	135 (48.2)
		11-80	136 (48.6)
Neutrophil (%)	274	< 40	18 (6.6)
		40 - 70	26 (9.5)
		> 70	230 (83.9)
Lymphocyte (%)	274	< 20	240 (87.6)
		20 - 50	27 (9.6)
		> 50	7 (2.6)
Hemoglobin (g/dl)	287	<7	12 (4.2)
		7-9	24 (8.4)
		10-12	29 (10.1)
		>12	222 (77.4)
Platelet count (x10^3)	287	<150	63 (21.9)
		150-450	215 (74.9)
		>450	9 (3.1)
Alkaline phosphatase (U/L)	120	≤150	84 (70.0)
		>150	36 (30.0)
Alanine transaminase (U/L)	162	≤ 50	150 (92.6)
		>50	12 (7.4)
Aspartate aminotransferase (U/	161	≤ 40	67 (41.6)
		>40	94 (58.4)
Estimated Glomerular filtration rate using (ml/min/1.73m^2)	239	< 1.2	157 (65.7)
		≥ 1.2	82 (34.3)
	237	< 15	20 (8.4)
		15-29	15 (6.3)
		30-59	49 (20.7)
		60-89	69 (29.1)
		>90	84 (35.4)

Table 6: Types of imaging modalities used in patients who died of COVID-19 in Oromia region, Ethiopia from April 2020 to November 2021

S.N	Imaging	n (%) N= 454
1	Chest x-ray	174 (38.3)
2	Abdominal ultrasound	52 (11.5)
3	Echocardiography	39 (8.6)
4	ECG	18 (4)
5	Computerized tomography scan	15 (3.3)
6	*Other	3 (0.7)

* *Doppler ultrasound, Cystourethrography*

Table 7: Frequency of chest x-ray findings

Chest x-ray finding	n (%) N=173	Chest x-ray finding: site of involvement	n (%) N=173
Opacity	76 (44)	Bilateral	89 (51)
Consolidation	17 (10)	Lower lung zone	21 (12)
Infiltration	13(8)	Upper lung zone	5 (3)
Effusion	7 (7)	Middle lung zone	4 (2)

Discussion

In this study, we aimed to describe the sociodemographic characteristics, clinical and laboratory profiles, and management of COVID-19 cases who died during inpatient treatment in the Oromia region of Ethiopia. Death was more common in the male population compared to females, and hypertension is the most common comorbidity, which is consistent with other studies [8, 10, 13, 17-20].

In this study, we found that the age group of patients who died was younger compared to other studies. The mean age of patients was 57 years, which is relatively younger compared to other studies [10, 20, 21]. However, the mean age is lower than this study in a single-center study conducted in Iran [19]. Similarly, the population's median age, which is 60 years, is relatively younger in our study compared to other studies in China [17, 18].

This study's median length of hospital stay before death was comparable to that in the Netherlands and East India, where it was six days [22-24]. However, another study conducted in Iran reported a higher median length of stay at 8 days [19]. In this study, the proportion of smokers is much lower, which is 0.9% compared to the study conducted in Illinois state, which reported that 39% of patients were current or former smokers and 4.3% reported in a study of Saudi, Jaza [10, 18]. In the same way as this study, the study conducted in Saudi reported all smokers who died due to COVID were male [10].

In this study, most patients who died from COVID-19 presented with symptoms such as cough, shortness of breath, and fever. These findings are consistent with other studies [8, 10]. However, while fever was the most common symptom reported in other studies [17, 19, 25], this was not the case in this study. This might be due to the absence of full documentation of temperature in this study in comparison to other vital sign components.

In this study, most patients who died from COVID-19 had a systolic blood pressure record of < 140 mmHg and diastolic blood pressure of < 90 mmHg. These values were higher than those reported in a study conducted at the Ethiopian Millennium COVID-19 care center [13].

In this study, about half of the patients (48.6%) had leukocytosis, with a white blood cell count of greater than 11,000 per µL. The majority of the cases showed a predominance of neutrophils and lymphopenia. Platelet counts were within the normal range for most patients. These findings of leukocytosis with lymphopenia are consistent with other studies [10, 17, 26]. However, unlike a study conducted in a Saudi Arabia Jaza, most of the patients in our study had elevated hemoglobin [10].

In this study, most patients had normal creatinine levels, consistent with other studies' findings. Glomerular filtration rate (GFR) is usually accepted as the best overall index of kidney function in health and disease [27]. In this study, about 15% of patients had an estimated GFR (eGFR) of less than 30 ml/min/1.73m2. This is higher than the proportion reported in Spain, where about 10% of patients who died from COVID-19 had stage 4 chronic kidney disease [26].

Most of the liver function tests were within the normal range or slightly elevated, which is consistent with findings from other studies [17, 26]. However, we have found alanine transaminase had decreased in our study. According to the Ethiopian national guideline, a chest x-ray is recommended as a suggestive imaging modality for classifying patients as probable cases. It was done for 18 (4%) patients in this study [28].

In this study, patients who died from COVID-19 were treated with higher-generation antibiotics, including 3rd and 4th-generation cephalosporins. This is similar to the study conducted in China, where higher-grade antibiotics such as carbapenem and linezolid were used [17]. However, this study did not treat patients with antivirals and intravenous immunoglobulin.

Conclusion

In this study, we analyzed 454 deaths due to COVID-19 from nine health facilities in the Oromia region. The death rate was higher among males and individuals older than 60 years. Most patients who died had at least one comorbidity, with hypertension being the most common. The median length of stay before death was five days. Most patients presented with cough and shortness of breath. Almost all of them required some

form of respiratory support upon presentation to the treatment center due to tachypnea and low oxygen saturation. However, chart reviews revealed incomplete records for patient follow-up, with complete records found for only 66% of patients on their second day of admission. Therefore, it is important to ensure adequate supplies of respiratory support for COVID-19 treatment centers and to maintain complete records of patient charts during consecutive follow-up periods.

Declarations

Acknowledgement

We wish to express our gratitude to the Fenot Harvard project and the Oromia Regional Health Bureau's Public Health Emergency Management for their invaluable support. Additionally, we would like to convey our appreciation to the data collectors for their collaboration throughout the data collection.

Ethics consideration

Ethical approval was obtained from the Oromia Health Bureau internal review board.

Authors contribution

TS, EKG, MW, DG, TN and DN conceptualized and designed the study and supervised all aspects of the study. TS, TT and KK performed the statistical analysis and interpreted the data. TS, EKG, MW, DG, KK, TT, TN and DN Drafted the manuscript, contributed to the literature review and provided critical revisions to the manuscript for important intellectual content. TK, ZM participated in the conceptualization and design of the study, drafted manuscript, and contributed to the literature review. All authors read and approved the final version of manuscript.

Conflict of interest

The authors declare that they have no known competing interests.

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We have not received any fund for this study.

Data availability

Data can be shared up on request

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Case Report

Concomitant Spontaneous Hemothorax and Perinephric Hematoma: Rare Presentation of Renal Cell Carcinoma

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Abstract:
Spontaneous hemothorax and perinephric hematoma are rare presentations of renal cell carcinoma. We present the case of a 30-year-old female who presented with progressive fatigue and weight loss over a 2-month period. Initially, she was suspected to have empyema and received anti-tuberculosis therapy at a local hospital. However, further evaluation revealed a low hemoglobin level and a CT scan showed a right renal mass with lung metastasis, along with massive hemothorax, perinephric, and retroperitoneal hemorrhage. She underwent surgical management with radical nephrectomy and evacuation of the hematoma. Pathological examination of the surgical specimen confirmed renal cell carcinoma. After treatment, the patient was discharged in stable clinical condition.

***Keywords**: Perinephric hematoma, hemothorax, renal cell carcinoma, case report*
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Introduction

Isolated perinephric hematoma and hemothorax can arise from various underlying clinical conditions (1). Concurrent presentation of spontaneous hemothorax and perinephric hematoma is reported following treatment with anticoagulants and it is a very rare entity in renal cell carcinoma. Metastatic renal cell carcinoma most commonly presents with solitary or multiple lung nodules followed by bone, lymph node and liver metastasis (2). This case highlights a rare presentation of concurrent perinephric hematoma and hemothorax in a patient with renal cell carcinoma (RCC).

Case presentation

A 30-year-old female patient arrived at the emergency department complaining of shortness of breath and easy fatigability of one day duration. She had been previously admitted to another hospital a month and two weeks prior with a history of cough, significant weight loss, and easy fatigability that persisted for over a month. Before her transfer to our institution, she had received 4 units of packed red blood cells (RBC) and had started anti-tuberculosis treatment with presumptive diagnosis of TB empyema. Despite this treatment, her weight loss continued to progress, and she showed no response to the anti-TB regimen. Consequently, she was referred to our hospital for decortication of the right-sided loculated collection.

Upon admission, the vital signs were mildly deranged with respiratory ate of 28 breaths/min and oxygen saturation of 80-85%. Blood pressure was 100/70 mmHg, pulse rate of 90 beats/min and Temperature of 36.5°C upon initial evaluation. She was given intra-nasal oxygen and the oxygen saturation was corrected. On general physical examination she had absent air entry in the right lower two thirds of the chest. Her baseline complete blood count (CBC) showed mild anemia with hemoglobin of 10.0 g/dL, with other CBC parameters within normal limits. Urine analysis showed microscopic hematuria. Organ function tests and coagulation profile were within normal limits.

To better evaluate the right pleural cavity collection, a chest CT scan was performed. It revealed a massive hematoma in the right pleural cavity with multiple bilateral lung nodules. An attempt was made to insert a chest tube to evaluate the hematoma, but it was unsuccessful and the patient was transferred to the surgical ward for further management. After admission, her fatigue worsened and she developed vaginal bleeding, hematuria, and right upper quadrant pain. An abdominopelvic ultrasound showed an empty uterus with a right renal

mass, along with perinephric and retroperitoneal collection. A cystoscopy evaluation revealed the bladder lumen was full of clot. She received multiple transfusions of packed RBC.

Following the abdominal ultrasound findings, an abdominopelvic CT with renal protocol was performed, which showed a right renal mass with perinephric and sub-capsular hematoma extending into the pelvic retroperitoneal space. The main renal vessels were normal, and no extravasation was observed on the delayed image.

Due to progressive bleeding and a decline in her hematocrit level, she underwent surgery. Intraoperatively, hematoma adherent to the liver and the duodenum was found, along with a deep parenchymal laceration at the upper pole and a solid renal mass measuring 5cm x 6cm x 7cm. Hematoma evacuation and nephrectomy were performed, with the patient receiving 1 unit of blood transfusion during the procedure. Tissue sample for biopsy was taken the patient was transferred to the ward in stable condition. The biopsy finding revealed a clear cell type of renal cell carcinoma.

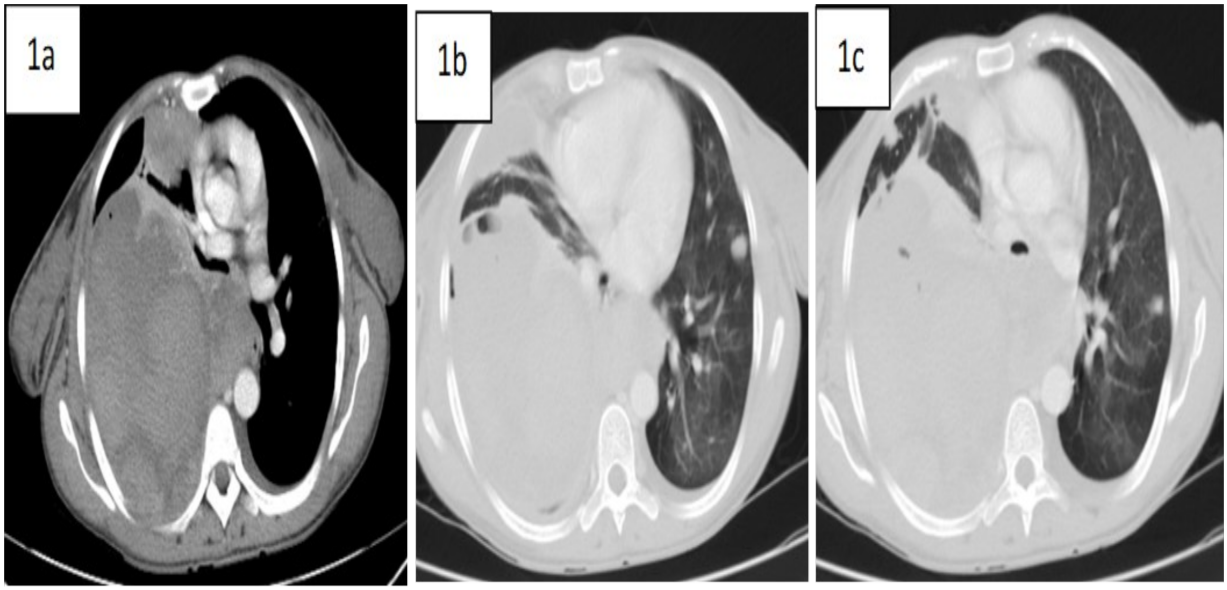
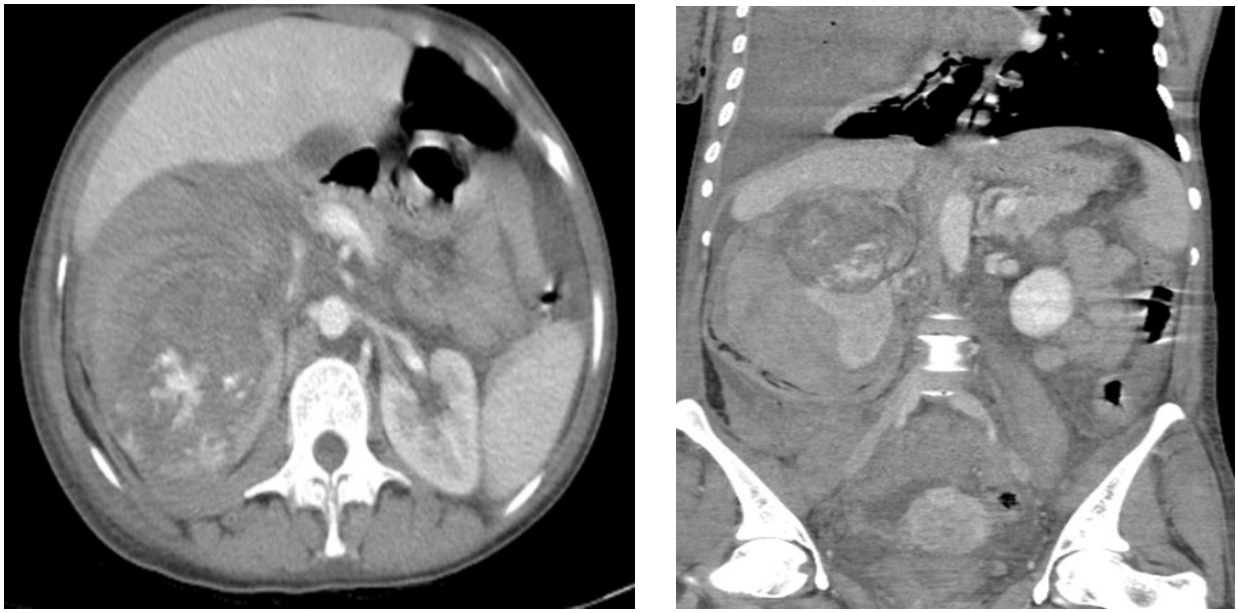


Figure 1: 1a) Post-contrast axial CT of the patient shows a heterogeneous hyper-attenuating collection in the right pleural cavity with no contrast enhancement, suggesting a massive hematoma collection that has compressed the adjacent lung parenchyma. A cannon-ball-type lung nodule is also visible in the visualized part of the right lung in a paracardiac location. Axial lung window chest CT at different levels (1b and 1c) show bilateral rounded lung nodules.



2a 2b

Figure 2: 2a)The arterial phase of the contrast enhanced axial CT image shows the right upper pole renal mass measuring 7cm craniocaudally. There are hyperenhancing areas suggesting the mass is hypervascular, with a surrounding hyperdense collection from a perinephric hematoma. b) The coronal pre-contrast CT scan shows the hematoma extending to the pelvic retroperitoneal space. The right hemothorax is also partly visible.

Discussion

Spontaneous hemothorax and perinephric hematoma are rarely documented in medical literature, and their occurrence as a result of RCC is notably uncommon. To the best of our knowledge, the simultaneous presentation of spontaneous hemothorax and perinephric hematoma secondary to renal cell carcinoma is extremely rare.

The etiologies of spontaneous hemothorax and perinephric hematoma differ significantly. Spontaneous hemothorax is primarily attributed to spontaneous hemopneumothorax, with other causes including coagulopathy, vascular disorders, and neoplastic causes (3). On the contrary, the leading cause of spontaneous perinephric hematoma, also known as Wunderlich syndrome, is primarily renal tumors (4, 5). Concurrent spontaneous hemothorax and perinephric hematoma have been reported following anticoagulation therapy (1). Metastasis of RCC presenting with hemothorax is exceedingly rare. In contrast, RCC can manifest with pleural effusion in approximately 1-2% of cases, a much more common occurrence than hemothorax. The most frequent pulmonary manifestation of RCC is metastasis to the lung, typically appearing as solitary or multiple lung nodules, as observed in our patient. Furthermore, RCC commonly metastasizes to sites such as bone, lymph nodes, liver, and the brain (2).

The etiology of spontaneous hemothorax and perinephric hematoma in RCC is not known. In a case report by Chetcutti and his colleagues, the mechanism of hemothorax was thought to be secondary to tumor invasion of the intercostal vessels and the vascularity of the tumor (6). Polkey, in his review of nontraumatic perirenal and renal hematomas, proposed that perinephric hematoma in RCC can result from venous congestion of the kidneys, with the resultant elevated vascular pressures and possible capsular rupture (7). Contrast-Enhanced Computed Tomography (CECT) is the most reliable modality in diagnosing retroperitoneal hemorrhage and RCC. (8) However, the accuracy of CT in diagnosing small tumors <2cm in size in the background of perinephric hematoma is poor, as evidenced by research conducted by Kendal et al, which found that 60% of patients with perinephric hematoma in the absence of anticoagulants and trauma had renal tumors that were not diagnosed on CECT or angiography (9) . The clinical presentation in this case was atypical for RCC, prompting consideration of other differential diagnoses during the patient's workup. Given the complaint of vaginal bleeding, choriocarcinoma with metastasis to the lung and right kidney was among the differential diagnoses considered. The patient's

reproductive age group made gestational choriocarcinoma a more plausible consideration(10); however, there was no recent history of abortion, molar, or non-molar pregnancy, and ultrasound and CT scan findings indicated a normal uterus. Another consideration was lung cancer with metastasis to the kidney, although less likely due to the presence of multiple lung nodules of similar size with cannonball appearance. While perinephric hematoma from adrenal metastasis of lung cancer has been reported, the likelihood of renal metastasis with perinephric hematoma is very rare (11). The final diagnosis in this patient was confirmed following histopathology results. The management of both perinephric hematoma and spontaneous hemothorax mostly depends on patient stability. For stable patients with spontaneous hemothorax, thoracoscopic draining is the optimal management option. For patients who are hemodynamically unstable or if the rate of bleeding is more than 500 mL/hr in the first hour with 200-300 mL/hr subsequently, an early surgical approach is preferable (3).

Following initial CT assessment, radical nephrectomy emerges as the preferred treatment for renal tumors identified as malignant, as delaying management could compromise resectability. Certain studies advocate for radical nephrectomy in cases of perinephric hematoma with a normal contralateral kidney, given the heightened likelihood of occult tumors (9). In instances of benign renal masses, embolization may serve as a viable alternative management strategy (12). In conclusion, the co-occurrence of spontaneous hemothorax and perinephric hematoma is observed in patients undergoing anticoagulant therapy. This case serves as an illustration of a rare presentation of RCC associated with spontaneous hemothorax and perinephric hematoma. Therefore, keeping in mind the possibility of potential underlying malignancy in patients exhibiting these clinical manifestations is crucial. Patients can be managed aggressively with a surgical approach or embolization or with delayed management after stabilization depending on their hemodynamic stability.

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Case Report

Gluteal Abscess Caused by Infected Gouty Panniculitis: A Case Report on Sequalae of Uncontrolled Gout

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Abstract:

Gouty panniculitis is uncommon manifestation of gout associated with monosodium urate (MSU) deposition into subcutaneous tissue. We report our local experience of this disease and its management strategy. Our patient was 39 years old gentleman, known to have gout who had not been compliant to follow up, presented with bilateral gluteal swellings for one month associated with discharge from the left gluteal swelling for 2 days. Clinical diagnosis of gluteal abscess with suspected infected gouty tophi was made. Wound debridement of infected left gluteal swelling was performed, followed by short course antibiotic therapy according to culture and sensitivity. Subsequently our rheumatology colleagues had assisted us with medical management of his gout, in which his right gluteal swelling did not get worsen and he remained well during our follow up.

Keywords: *Gouty tophi, Panniculitis, Monosodium urate crystals*
Citation : *Tan SS, Kyi KW, Gluteal Abscess Caused by Infected Gouty Panniculitis: A Case Report on Sequalae of Uncontrolled Gout Ethiop Med J 62 (3) 127-132*
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Introduction

Hyperuricemia associated with monosodium urate (MSU) crystal deposition in the synovial fluid leads to a condition known as gout, a form of inflammatory arthritis (1). Diagnosis of gout is proven by identification of MSU crystal in synovial fluid analysis (1,2). Gout is getting more prevalent related to diet factors (3). Gout affects men more than female (ratio 4:1) (1). The presence of MSU crystals in synovial fluid or tissue biopsy confirm diagnosis of gout (4). Tophi characteristically resembles granuloma where inflammatory cells and connective tissue surrounding the MSU crystals aggregate (4,5), which suggests advanced stage of gout. Common sites of tophi include tendons, ligaments, knee joints and so on (6). There were reports of unusual sites of tophi, namely skin, bones, and axial skeletons (7).

Gouty panniculitis occurs due to deposition of urate crystals into subcutaneous tissue, either prior or as a sequalae of chronic tophaceous gout (1,9). It was hypothesized that subcutaneous tissue destruction and localized inflammation leading to increased production and deposition of uric acid into subcutaneous layer (9).

We would like to share our experience of encountering a case of atypical site of gluteal gouty panniculitis which manifested with abscess formation.

Case presentation

This is 39 years old gentleman, with underlying hypertension and gout previously on allopurinol who defaulted follow up for the past 1 year. He presented with bilateral gluteal swelling of 1 month associated with discharge from the left gluteal swelling for 2 days. Clinical examination revealed multiple indurations on the right gluteal region, ruptured left gluteal swelling about 8cm x 10cm with chalky white material and purulent discharge surrounded by erythematous skin (Figure 1).

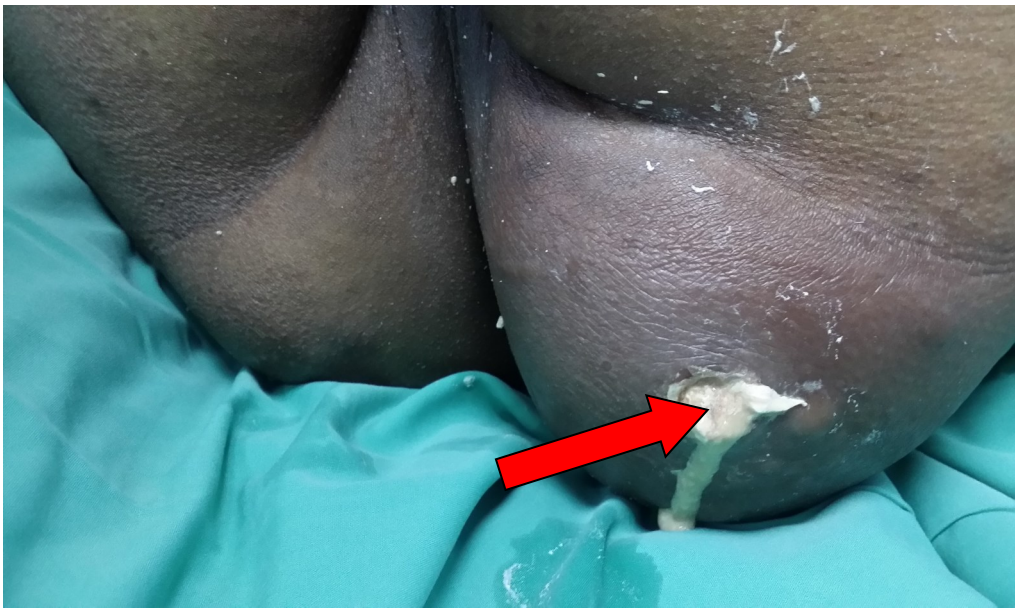

Figure 1: Photo of left gluteal region showing erythematous skin and induration with ruptured swelling showing chalky material suggestive of tophi (red arrow)

Total white cell count was raised (36.3 x 103/µL), with deranged urea (12.5 mmol/L) and creatinine (290 µmol/L). His serum uric acid was 723 µmol/L.

He underwent wound debridement of left gluteal infected gouty tophi (Figure 2)

and subsequently referred to rheumatology team for uncontrolled gout. He was started on low dose hydrocortisone and allopurinol for severe unstable chronic tophaceous gout.

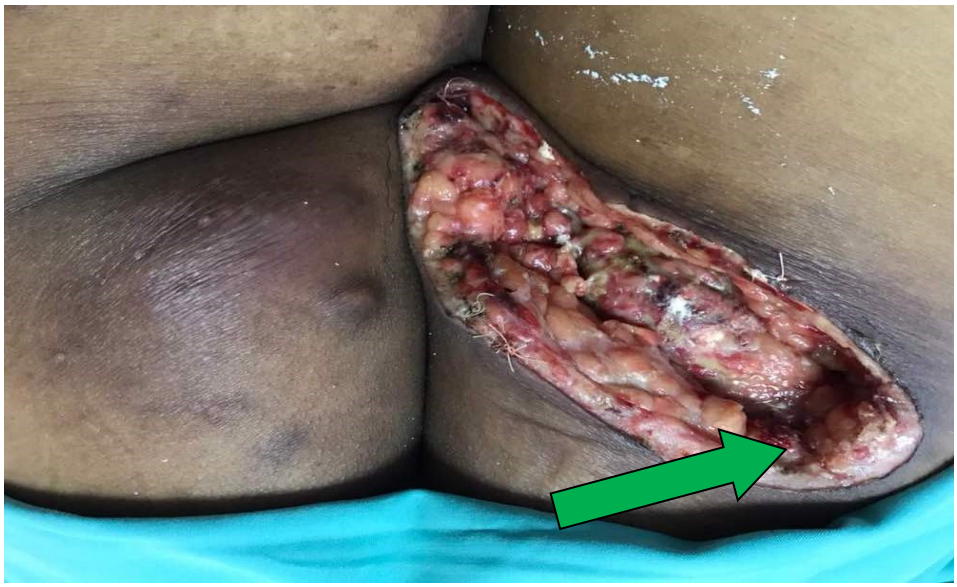

Figure 2: Post wound debridement of left gluteal region showing underlying healthy muscle and fascia, with minimal residual tophi. (**green arrow**)

Post operatively he has had daily saline dressing over his left gluteal wound and his intra operative culture reported as *Staphylococcus aureus*, which he had completed 1 week course of antibiotics. Histology of left gluteal tissue reported palisading granuloma showing aggregates of histiocytes with foreign body type multinucleated giant cells, consistent with panniculitis (Figure 3).

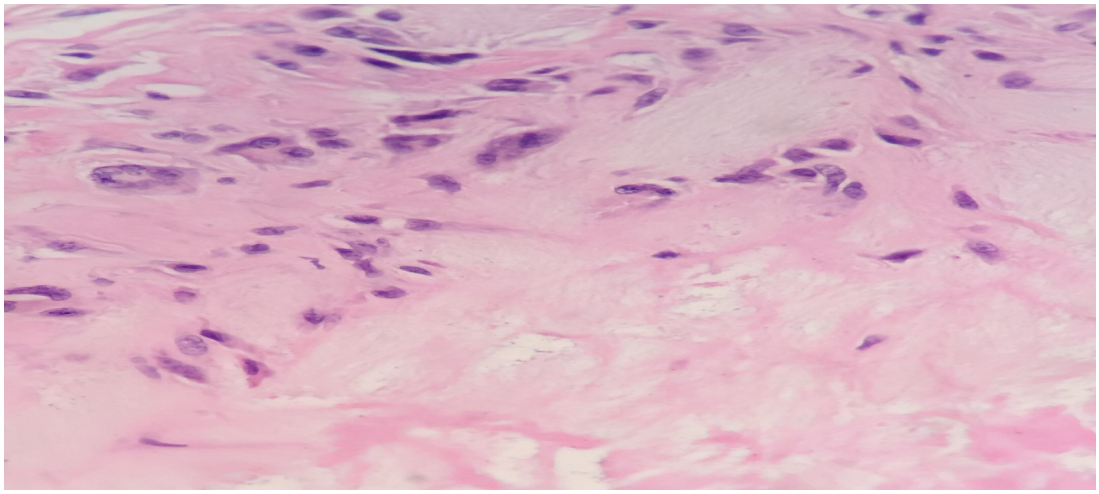

Figure 3: H&E x 200 - The palisading granuloma shows aggregates of histiocytes with foreign body type multinucleated giant cell.

On follow up after 3 months, he had his left gluteal wound almost healed with granulation and re-epithelialization seen, with no worsening of his right gluteal swelling as he had been compliant to his gout medication (Figure 4).

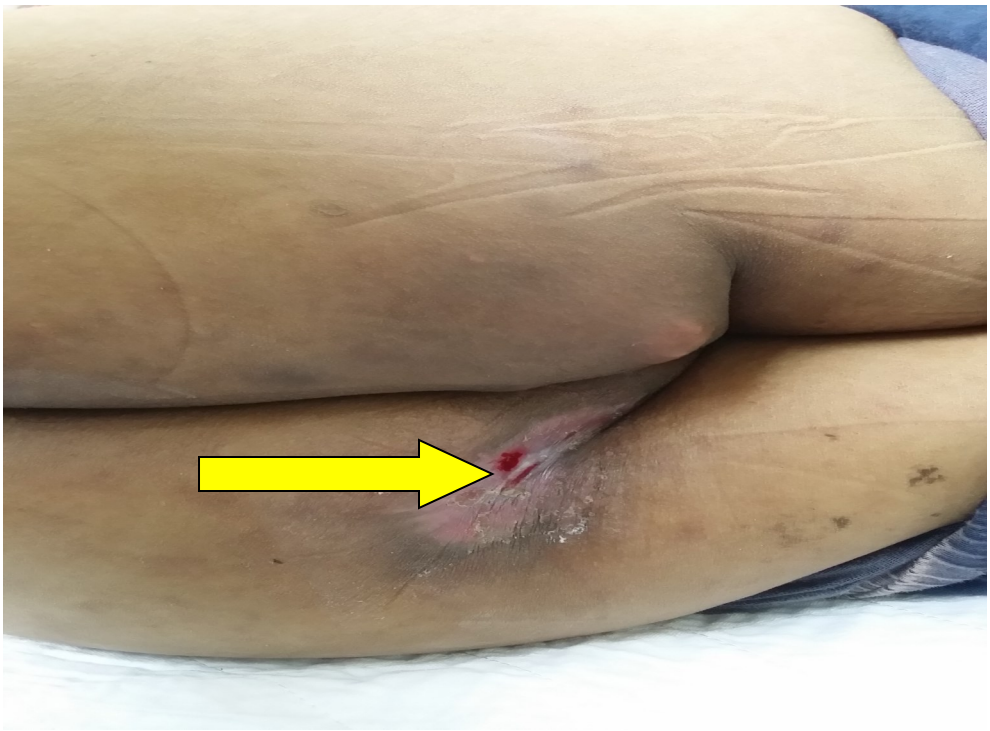

Figure 4: At 3 months follow up, there is evidence of granulation and re epithelization of left gluteal wound. Right gluteal gouty tophi not worsened compared to previous. (**yellow arrow**)

Discussion

Gouty panniculitis is atypical presentation of gout patients with subcutaneous tissue lesions at any site, related to lobular hypodermis deposition of MSU crystals (8,9). This is uncommon diagnosis unfortunately happened to our patient, with paucity of reported cases till present (10,11). There was postulate that high tendency of deposition in lobular subcutaneous tissue possibly related to microtrauma of the terminal capillary wall and adipose tissue coupled with MSU crystals associated arteriopathy (9). Our patient presented with significantly elevated uric acid level, which might be associated with occurrence of gouty panniculitis (12).

Differential diagnoses of gouty panniculitis include cellulitis, pseudogout, calciphylaxis, lupus panniculitis, which need to be excluded (13). Panniculitis is a histological diagnosis, with presence of granuloma with adipocyte necrosis (10), which is found in our patient histopathological specimen. Whenever diagnosis is in doubt or uncertain, imaging modalities (ultrasound, plain radiograph, computed tomography, and magnetic resonance imaging) can be useful to identify severity of disease (14). The presence of chalky whitish material from our patient buttock with background history of gout supported our clinical diagnosis of infected gluteal gouty tophi, thus we did not proceed with any imaging studies, as it is considered as a form of subcutaneous infection of unusual etiology.

In our patient, surgical treatment in the form of wound debridement was performed, followed by anti -hyperuricemic medication, with low dose steroid, comanaged with our rheumatology colleagues, aiming to control pain and inflammation of contralateral gouty tophi (9,10).

While our case report is limited by lack of structured guideline in managing gouty panniculitis with scarce literatures, we were glad that collaboration between surgical and rheumatology professionals provide good post operative outcome for our patient. We had proven that with adequate wound debridement followed by compliance to anti-hyperuricemic medication by our rheumatology colleagues, provide long term uric acid control and showed no new gouty tophi elsewhere in our patient.

Conclusion

In patients known to have long standing hyperuricemia and gout with subcutaneous erythematous lesions, clinicians should consider gouty panniculitis as a possible diagnosis. Surgical intervention for infected lesion, coupled with medical therapy to control hyperuricemia can be useful treatment strategy to prevent recurrence.

Competing interests

There was no funding for the study and no conflicts of interest to disclose.

Consent

Written informed consent was obtained from the patient participant for publication of this case.

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Case Report

Hemorrhoids or Malignant Melanoma? A Case Report

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Abstract:
Anorectal malignant melanoma (ARMM) is an aggressive and rare tumour. It carries a poor prognosis due to its inherent aggressive systemic activity and advanced disease at the time of diagnosis. Surgery is the mainstay treatment which ranges from wide local excision to abdominoperineal resection (APR). Neither chemotherapy nor radiotherapy has proven benefits in increasing survival rate or reducing loco-regional recurrence. In this case report, we present a 52-year-old male patient with anorectal melanoma. Staging scans showed an anorectal tumour with nodal involvement. He underwent laparoscopic abdominoperineal resection in Hospital Taiping, Malaysia. He was discharged home well postoperatively.

***Keywords**: Anorectal malignant melanoma (ARMM), Abdominoperineal resection (APR)*
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Introduction

0.5-4% of malignancies in anorectal region are caused by ARMM, making it an extremely rare entity[1]. They are usually diagnosed among the population in their fifties and sixties with higher predisposition in females. Clinical presentation of ARMM can be non-specific. In up to one-third of cases, these lesions are mistaken for haemorrhoids or benign rectal polyps. In this article, we share our experience in managing ARMM and complement this with a brief review of the literature

Case Report

A 52-year-old male with no known medical illness complained of painful defecation tenesmus and per rectal bleeding for 1 year. He had a history of seeking treatment at a general practitioner and was treated as a haemorrhoid. Clinically there was no abdominal mass or inguinal lymph nodes palpable. A digital rectal examination showed a distal rectal mass about 3 cm from the anal verge. Colonoscopy showed a low rectal tumour about 3 cm from the anal verge with no synchronous tumour found. A biopsy of the tumour revealed melanoma. A staging computed tomography thorax, abdomen, and pelvis were done for him which showed low rectal mass with bilateral lung nodules of an indeterminate nature. Pre-operative MRI showed an anorectal tumour 1.5 cm from the anal verge with enlarged mesorectal lymph nodes. Two enhancing lymph nodes were seen over the right external iliac and left internal iliac. The radiological staging was T4b MRF+N2M0. He then underwent laparoscopic APR with an extra peritoneal sigmoid colostomy. He made an uneventful recovery. Histopathological examination of the specimen is consistent with mucosal melanoma of anus. The stage of the disease was T2N1(2/21) M0 with circumferential resection margin involvement.

Figure 1: shows an APR specimen that has been cut open at the distal end revealing a fungating tumour. It measures about 3.8x2.7x2cm and has a dark brownish appearance.

Discussion

The diagnosis of ARMM remains difficult and requires a high index of suspicion due to its lack of pathognomonic features. Histology and immunochemistry remained the accurate diagnostic tools to confirm the diagnosis of ARMM.

Anal melanoma is usually suspected when brown or dark mucosal lesions invade the dentate line. However, up to one-third of malignant melanoma are non-pigmented. In cases where the diagnosis of ARMM is in doubt, Immunohistochemical evaluation using proteins such as SOX 10, HMB-45, Melanin A, and S 100 are indicated[2]. All of which were found in the immunohistochemistry examination of this patient.

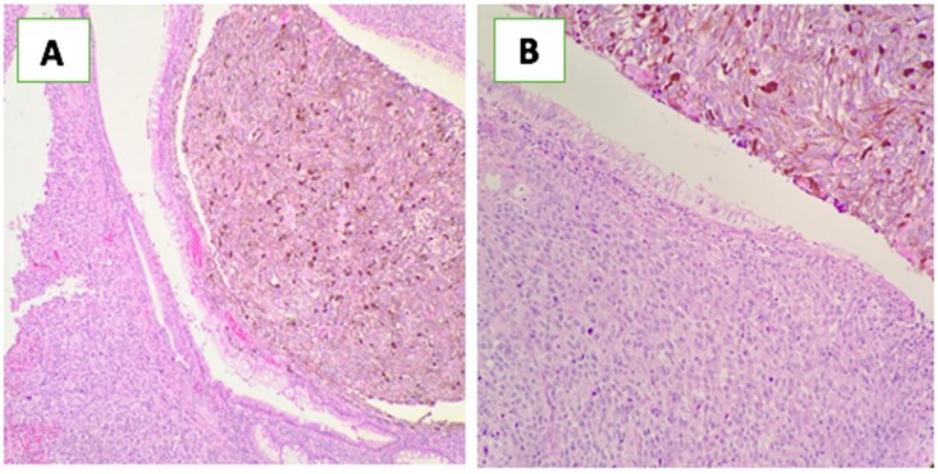

Figure 2: Mucosal melanoma of anus. A) Melanoma arising within anorectal mucosa. (H&E; x40) B) Malignant cells disposed of in diffuse sheets with marked nuclear pleomorphism and cytoplasmic fine melanin pigments. (H&E; x200)

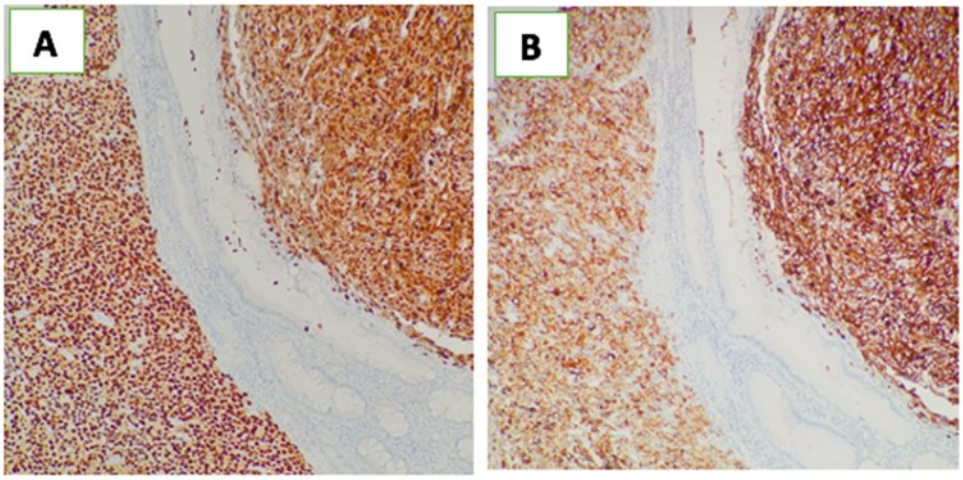

Figure 3: Immunohistochemistry study in mucosal melanoma of anus. (A) Nuclear positivity for SOX-10. (B) Cytoplasmic staining for HMB45.

Imaging studies such as computed tomography thorax, abdomen, and pelvis are usually done to assess for any evidence of distant metastasis and follow-up. MRI pelvis is also another important tool for disease staging and planning for surgery. ARMM is staged based on loco regional and distant metastasis. About 20% of patients with ARMM present with lymph node metastasis and 10% with distant metastasis at the time of diagnosis with a 5-year survival rate of about 20%[4]. ARMM is an aggressive malignant neoplasm that tends to metastasize early in the course of the disease. Coupled with the lack of specific clinical features and non-specific symptoms, the patient tends to present late when their symptoms fail to improve after presumably being treated for a benign cause. This leads to an overall poor prognosis.

Surgical resection has been the standard of care for ARMM. However, whether abdominoperineal resection (APR) or wide local excision (WLE) is the most appropriate surgical approach is still a debatable issue. There is no clinical trial to date that proves one method is superior to the other in terms of long-term survival due to the rarity of this disease. APR is thought to achieve a higher curative rate and better regional control while WLE is more favourable for its minimal invasiveness. However, R0 resection cannot be achieved with WLE if there is mesorectal and mesenteric lymph node metastasis [2]. In patients with locally advanced disease, it is also difficult to achieve R0 resection as there is no neoadjuvant treatment to downsize and downstage the tumour. The rate of recurrence is lower in radical surgery but there is no significant difference in prognosis in patients who underwent APR or WLE. Hence, treatment of ARMM should be individualized based on patient comorbidity and functional outcomes.

Conclusion

ARMM remains a malignancy with a very poor prognosis. Due to its rarity, there has not been a standardized treatment protocol for this illness since its discovery. The approach to surgery (WLE versus APR) remains debatable.

Consent

Patient verbally consented to put his case for educational purpose.

Conflict of interest

none

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