ISSN: Print -0976-9234

Journal of Pharmaceutical Negative Results

Volume No. 17
Issue No. 2
May - August 2025

ENRICHED PUBLICATIONS PVT. LTD

JE-18, Gupta Colony, Khirki, Extn, Malviya Nagar, New Delhi-110017
PHONE : - + 91-8877340707
E-Mail : info@enrichedpublications.com

ISSN: Print -0976-9234

Journal of Pharmaceutical Negative Results

Aims and Scope

Journal of Pharmaceutical Negative Results (www.pnrjournal.com) [ISSN: Print -0976-9234, Online - 2229-7723] – (An official publication of Association of Indian pharmacist-AIP, Published by ResearchTrentz). The journal is a peer-reviewed journal developed to publish original, innovative and novel research articles resulting in negative results. This peer-reviewed scientific journal publishes a theoretical and empirical paper that reports the negative findings and research failures in pharmaceutical field. Submissions should have a negative focus, which means the outputs of research yielded in negative results are being given more preference. All theoretical and methodological perspectives are welcomed. We also encourage the submission of short papers/communications presenting counter-examples to usually accepted conjectures or to published papers. This Journal is a biannual publication.

ISSN: Print -0976-9234

ISSN: Print -0976-9234

Journal of Pharmaceutical Negative Results

(Volume No. 17, Issue No. 2, May - August 2025)

Contents

ISSN: Print -0976-9234

Environmental Damage And Fundamental Changes In Civil Liability (Iran And The European Union)

1Hossein Valizadeh, 2Nejatollah Ebrahimian*, 3Sharareh Mofidian
1Ph.D, Department of Law, Central Tehran Branch, Islamic Azad University, Tehran, Iran Hossinvalizadh80@gmail.com 2*Assistant Professor, Department of Law, Central Tehran Branch, Islamic Azad University, Tehran, Iran 1344ne@gmail.com 3Assistant Professor, Department of law, Central Tehran Branch, Islamic Azad University, Tehran, Iran Dr.sharareh.mofidian@gmail.com
DOI: 10.47750/pnr.2022.13.04.270

A B S T R A C T

This study examines the changes in the foundations of civil liability for environmental damages in the Iranian and European Union (EU) law. This is fundamental, descriptive-analytical research implemented with the library method through note taking. The importance of analyzing this issue is evident from the clear tendency of the laws of most European countries to accept and recognize absolute civil liability instead of fault-based civil liability in important documents approved at the EU level. In the current research, changes in the basics of civil liability for environmental damages have been investigated in two general areas of substantive and formal changes. The substantive changes could be classified as "privatization" and "collectivism" of civil liability for environmental damages. On the other hand, formal changes can be regarded as "absolutism and despotism" in civil liability for environmental damages as well as "an evolution in the demonstrative evidence system regarding civil liability for environmental damages". Due to the destructive consequences of environmental damages for people's daily lives, many legal systems tend to take the responsibility of affirming these damages from the judicial authority. It is assumed that harmful behavior is committed, and it is the defendant who must prove that he/she did not commit such behavior or without an emergency reason. This could be the most important development in the civil liability system for environmental damages in the European Union. The outstanding result of this study is that the European Union has experienced important developments in regulations regarding the protection of the environment and is executing instructions while Iran's laws are far from these developments.

Keywords: environmental damages, Iranian law, the European Union law, absolute liability, collective liability

INTRODUCTION:

Close analysis of the civil liability in Iranian laws and international documents shows that the traditional civil liability rules are not efficient for compensating environmental damages since it is based on fault, and the law of civil liability is not responsive to general interests and rights since it simultaneously supports private rights and properties. Some jurists expand environmental damages to include harm to properties, individuals, and the environment itself, which disrupts the environmental balance. Therefore, the custodians and users of environmental elements are considered the victims of

ecological damages, and therefore they can file a lawsuit and demand compensation because any type of pollution is considered a violation of human rights and is a kind of fault. The traditional civil liability system is based on the theory of fault. In general, three cases are considered in the theory of fault. First, innocence is in priority, meaning that if someone has committed an act and damage is caused, his innocence is emphasized, not his responsibility for causing the damage. Second, proof of guilt is required to convict the agent, and finally, the agent must accept the fault.The theory of fault belongs to traditional societies, which do not fit the requirements of Iran's developing society. Its most important drawbacks are that it is tough to assess environmental damages; Second, proving the relationship between pollution and environmental damages is difficult and in some cases impossible; Thirdly, environmental damages have very little incentive to follow up and claim environmental damages, and finally, the condition for realizing civil liability, i.e. violation of individual property rights, is not provided. The reasons for the failure of the traditional rules of civil responsibility in this regard are that the victims of environmental damages have very little motivation to pursue and claim environmental damages. Proving casual elation as well as evaluating environmental damages is difficult and even in some cases it can be beyond the authority's ability. Since, in most cases, the components of the environment are not considered private properties of individuals, the condition for realizing civil liability, i.e. violation of individual property rights, will not be met.

Given the theory of civil liability regarding compensation for environmental damages, the injured party can get his rights if he proves that the agent committed a mistake, and the damage caused to him is a direct result of the agent's fault. The agent also has the opportunity to prove that the damage was caused by the fault of the injured party or due to a natural irresistible power to eliminate his liability. According to this theory, committing fault and error is the main condition of civil liability. In addition, in some legal systems, if the agent cannot recognize and is not capable of assigning a fault (like an unintelligent minor and insane), there will be no responsibility to compensate for the damage. In general, the remarkable feature is that this theory considers everyone responsible for the consequences of his actions and gives responsibility a personal aspect, which increases caution among people. It is influenced by criminal liability where committing a fault is the main condition of the individual's responsibility. The present research aims to examine the different legal opinions about civil liability for environmental damages compensation, and the place of fault in this type of liability to help better understand civil rights regarding environmental damages compensation. No research about civil liability for compensation of environmental damages with an emphasis on "the role of fault" has not been published. Substantive developments in the foundations of civil liability for environmental damages in the laws of Iran and the European Union

1. Collective civil liability for environmental damages

A major reason for making civil liability a collective liability is related to the definition presented in new discourses and approaches regarding the right to a healthy environment. In a comprehensive definition of this right, the right to a healthy environment refers to those rights established for protecting the quality of human life as well as the destruction of the biosphere and nature. In research, the right to a healthy environment is defined as follows: "The inalienable and unobjectionable human right by which every individual and all human beings collectively have the right to share and enjoy a healthy environment together with the collective responsibility of preserving its health to preserve human health (including present and future generation) and all-round development (economic, social and cultural)"1. This definition has taken into account the majority of the modern elements of the right to a healthy environment for several reasons. First, it has been introduced as a right. Second, it states that human beings collectively deserve to share and enjoy a healthy environment. Third, this right is combined with the collective liability to preserve it. Fourth, it has considered future generations and the issue of sustainable development. Therefore, except for some controversial elements – e.g., the owners of this right (individuals or society) and being the third generation or independent of this right from other human rights – this could be a suitable definition.

Of course, it should be noted that analyzes presented so far on the right to a healthy environment are based on the doctrines of the international law of solidarity and the transnational origins of collective rights. In other words, these analyzes are similar. Intellectual conflicts between collectivists and individualists have in turn affected these rights Analyzes have found a dual orientation based on an "individual basis" or "collective basis". This attitude was similar to the extensive fight of the defenders of the rights of the first generation (rights of freedom) and the rights of the second generation (rights of equality) in the years after World War II, while with the end of the Cold War, this conflict also ended and moved towards Solidarity rights.Several new rights claimed to have a collective nature, took a different path during the evolution of their rules, and were distinguished from the rights of their "companions". It is totally clear that the right to a healthy environment was first defined based on the teachings of international law and within the framework of transnational rules, and then entered into the constitution and national laws. The dominant theory that defended the international content of these rights was the "collective" nature of the right to a healthy environment, along with other collective rights including the right to peace, and the right to the common heritage of humanity. Competing analyzes, especially those related to the right to a healthy environment, were presented in the framework of a transnational understanding of this category of rights.

However, the subsequent developments revealed that the right to a healthy environment is not enough compatible with its initial analysis. The most important evolution that made this right independent was its entry into the domestic laws of countries and its recognition in domestic public law. Therefore, the

right to a healthy environment is completely distinct in terms of its entry into the rules of national law, compared to its fellow trains (i.e. solidarity rights). In domestic public law, the analysis of this right nature requires a "theoretical break" from the common and "habitual" analyzes of it in the texts presented so far. Currently, the right to a healthy environment has evolved in terms of nature and basis in domestic public law and cannot be accurately adapted to the previous common analysis. Contrary to the international analyzes of the environmental right and the criticisms of its nature in this framework, the right to a healthy environment has been consolidated in domestic public law and its "inconsistent", "collective" and "soft" nature is changed. In addition, with the recognition of this right in the constitution, ordinary laws and administrative and judicial procedures of it have become the claim of each citizen against the government, which ultimately benefits the entire human society, nature, and even future generations. Another reason relates to changing approaches regarding environmental damage in new discourses. Jurists have divided the damage into two distinct groups material and spiritual2. The third type, called collective damage, is less discussed but is crucial in the discussion of liability regarding the environment. That is, sometimes damage can hardly be limited to specific people. It is inflicted on an unlimited group and is so widespread that no one can consider himself the main victim and claim compensation3. Therefore, the damage comes to a population or a group of people without being able to identify a certain person to be the direct goal of this damage.

In the first paragraph of Article 2 of the Draft Principles (2006) regarding the International Law Commission, the damage is defined as "significant harm to persons, properties, and the environment, which includes the following:A- Harm to life or physical injury; b- Damage to property, including cultural heritage; c- Damage caused by a disturbance in the environment; D- Costs of usual measures to restore the former state to the property or the environment, including natural resources; E- Costs of common countermeasures. Damage is also defined in other international documents[4].

Therefore, damage means harm that occurred as a result of an act or omission of an act by a (real or legal) person, or natural disasters to individuals, properties, or the environment. This word has found different dimensions due to developments at any point in time and in different fields. Including the judgment of the "Trill Smelter" arbitration, Article 1 of the Paris Convention on Liability to Third Parties in the Nuclear Energy Field (1960), Article 1 Paragraph 7 of the Brussels Convention on the Liability of Operators of Nuclear Ships (1962) and the Convention on International Liability For damage caused by space objects (1972).In all these cases, the damage is defined as loss of life, personal injury, loss of property, or damage to it. Environmental damages/loss caused by risky actions, regardless of whether accompanied by physical injuries and financial losses, is independent of damage to persons and property[5].Therefore, international law has adopted a collective responsibility approach to support beneficial but risky activities for society, support innocent victims, and not impose heavy environmental damages on only one beneficiary.

More precisely, international law tries to compensate for damages in a group by obligating insurance or financial guarantees or establishing compensation funds. In fact, according to the realities of the international community, international law supports the sharing of social costs, and it seems logical that the responsibility resulting from non-prohibited actions is a form of sharing compensation for environmental damages. Also, compensation by the government leads to the social distribution of risk and benefits to social cohesion.After all, the understanding of the environment as a common global heritage is the basis of many theoretical discourses and practical actions aimed at protecting the environment. Regarding the global interest in the "protection of the world heritage", according to Article 4, each member of the convention has to ensure the "identification, protection, preservation, introduction and transmission of heritage located in its territory to future generations". This duty includes "all attempts to achieve this goal using the maximum resources and, if necessary, using any assistance and international cooperation".

In light of this understanding of the environment, operational guidelines have emphasized a close relationship with the World Heritage Convention and strengthened cooperation with other agreements. These conventions include the 1992 Convention on Biological Diversity, the 1979 Bonn Convention on the Conservation of Migratory Species of Wild Animals (CMS), the 1974 Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES), the Convention Ramsar about wetlands of international importance, especially as a habitat for waterfowl (Ramsar). In protecting biodiversity, none of these documents work alone.

In some international documents regarding environmental protection, the right to benefit from the environment is mostly considered an individual right, but in others, it is a collective right. For example, the Stockholm Declaration defines the right to a healthy environment as follows: "The right of man to enjoy freedom and well being and suitable living conditions in an environment that allows him to live with dignity and happiness." According to the African Charter of Human Rights, the right to a healthy environment is presented as an independent concept from other human rights and tries to make the right to a healthy environment an independent right for people. According to this document, the right to a healthy environment is "the right of the people to enjoy a satisfactory environment suitable for development". The important issue in this document is that, unlike the American Convention on Human Rights and the Stockholm Declaration, which considers this right for individuals, it considers the right to a healthy environment as a collective concept and belonging to "the people".Therefore, according to this charter, the right to a healthy environment is an inalienable and inalienable human right by which every human being and all human beings collectively have the right to share and enjoy a healthy environment along with the collective responsibility of maintaining the health of the environment to They have the preservation of human health (both of the current and future generations) and all-round development (economic, social and cultural).

This definition includes most elements of environmental rights. First, it is introduced as a right. Second, human beings collectively deserve to share and enjoy a healthy environment. Third, this right is combined with collective liability. Fourth, it attends to future generations and sustainable development. In addition, according to Article (24) of this charter, "all people have the right to enjoy a satisfactory environment that is suitable for their development." In fact, this article does not consider the right to a healthy environment as an individual human right, but rather a collective right given to all people. However, this issue does not prevent the African Commission on Human Rights, especially regarding recent events of violating this article and concerning other articles of the Charter, from interpreting this article in this specific way and imposing obligations on EU members to respect individual as well as collective rights.However, it should be remembered that the right to a healthy environment is considered collective due to the collective nature of solidarity rights. But like other rights of solidarity, it will not prevent citizens from benefiting from the rights individually and as a group. Of course, there are different opinions about whether individuals can independently benefit from solidarity rights in the same way as other human rights and have the possibility to claim. One view is that instead of individuals, it will be sufficient to identify the representative body of the society and give the responsibility of the demand to the government.

Consequently, even the so-called collective rights can be reduced to individual rights. In other words, people have the right to peace, the right to development, and the right to a healthy environment, but since the realization of these rights makes governments and groups (notindividuals) involved in its demand, they have found a collective nature.In domestic laws, even at the level of the constitution, as the most important legal text in any legal system, there are clear tendencies toward collective liabilities in preserving and protecting the environment. Specifying the necessity of environmental protection in the constitution can have various reasons, including the seriousness of environmental protection, and the wide and complex nature of environmental problems, which require collective political action to protect all members of society6. When environmental protection is defined as a norm in the constitution, the need for social attention to this necessity will be emphasized. Therefore, the need for collective

protection of the environment as well as the recognition of collective responsibility for environmental protection is highlighted again. A basic theoretical basis for such a belief is that if environmental values become a collective value, environmental protection benefits all these different groups, and if it is preserved, they will all benefit equally. Therefore, an important goal of the environmental protection system, along with culture building for transforming the environment as a collective value, should be to create a balance of the common interests in the environment7, which requires the development of a social justice system.

1. Privatization of civil liability for environmental damages

From a conceptual perspective, privatizing civil liability for environmental damages is based on the premise that not only governments are obliged to compensate for environmental damages, but also the private and non governmental sectors can and even should accept this obligation. The privatization of civil liability for environmental damages is justified by two reasons; First, it is more compatible with choosing the theory of risk as the basis of responsibility for compensation of cross-border damages caused by dangerous activities. In fact, according to this theory, the person who created the risk and seeks to gain economic benefits must bear the harmful results of controlling the activity. This person is the beneficiary of a harmful activity due to the dominance of the private economic system in the modern world. Second, the extent, irreparability, and unknown nature of many transboundary damages, especially environmental damages, have been effective in encouraging governments to remove responsibility for transboundary damages[8].

Privatizing civil liability for environmental damages has been partially introduced into the approach of Iran's legal system. Meanwhile, at the level of the European Union, more serious attention has been paid to this category and important documents have been approved by the European Union members.The most important aspect of identifying the privatization of civil liability for environmental damages in Iran is specifying the responsibilities of legal entities to protect the environment. The legislator may indirectly punish legal entities by ruling to prevent the establishment of polluting places, like the budget law of 1328, which, according to note 30, prohibits the establishment of factories and workshops in cities and their suburbs if they are injurious to health or disturb neighbors' conform. Sometimes legal entities are punished by punishing the manager of legal entities. For example, according to Article 568 of the Islamic Penal Code, in case of the destruction of historical and cultural property by legal entities, any of the managers and officials who give orders will be sentenced to the prescribed punishments. Although the principle of personal punishment has been accepted because the responsibility for the polluting activities of a company rests with its managers the responsibility of legal entities has been considered indirectly[9].

On the other hand, the European Commission in its amendment bill, imitating the Lugano Convention, assigns the responsibility to the "operator" or "beneficiary". In this document, a beneficiary is the one who supervises an activity.

In other words, the beneficiary is the response according to the principle of "the polluter must pay" and therefore is a person other than the owner or occupier of the contamination. In the proposed directive, a co-user is definedas a person who performs the activities mentioned in the directive. The definition of "beneficiary" was one of the most controversial topics among the commission, European Union members, and non-governmental organizations. It was generally agreed that a beneficiary is a person who has control over the harmful activity as the focus is on "practical control". From the directive view,

"beneficiary" is a natural or legal person, whether private or public, who executes or controls a professional activity, or if it is foreseen in the national law, he is the one with the decisive economic power over the operation and has the license for these activities; A beneficiary is a person who has direct control, i.e. is responsible for day-to-day management, not indirect control. Therefore, it does not include parent companies. Also, any economic enterprise that exploits an activity - even if it is practical - can be recognized as a beneficiary according to the directive[10].

In Article 7-161 of the French Environmental Liability Bill, which combines Articles 6-2 (Definition of Operator) and 2-7 of the Directive (about professional activities), "beneficiary is defined as follows: "Concerning the purpose of the European Community Legislator, the operator must be a person who can effectively and efficiently carry out preventive and remedial measures. Effective control in the context of the activity, job, or company means refers to a beneficiary's efficient management. This article does not include shareholders, credit institutions, government officials who are responsible for administrative control, and also official officials".Most countries with customary laws have accepted the responsibility of legal entities.However, several countries have rejected this responsibility. The argument of the opponents of liability for legal entities is that some types of punishment, including imprisonment, cannot be implemented for these people, while the supporting countries, including the European Council of Ministers, believe that financial and cash punishments should be used instead of imprisonment[11].

In penalizing legal entities, a point should be attended to: the financial penalty should be determined carefully since if it is very low, it may seem negligible compared to environmental pollution for the agent (e.g., a factory), and if it is very high, it may cause economic problems or even unemployment. A reasonable solution proposed by the European Council of Ministers is to deposit the obligation on behalf of legal entities. The obligation is an amount of money determined by estimate, or it is a specific amount of money determined by the judge for each day of delay in fulfilling the obligation, to oblige the different agents to perform it. It allows the judge to implement his decision. This punishment forces the polluter to quickly take the necessary measures to stop the pollution, otherwise, a heavy fine will be waiting for him[12].Another dimension that the European Union has focused on in the practical realization of the privatization of civil liability for environmental damages is social regulation. Regulation is a process in which the government allows or prohibits certain activities for individuals and companies. These activities are mostly private and sometimes public, and the government takes control of them through a continuous administrative process and generally through specific administrative organizations (regulatory organizations). Regulation, also called "organization", "regulation", "provision" or "adjustment", is a tool that largely expresses the interventionist effective presence of the government in social and economic relations. Governments monitor and control many products and services offered by tools[13].

Formal changes in the foundations of civil liability for environmental damages in the laws of Iran and the European Union

Absolute liability is a term used in Anglo-American law for liability based on no fault, which is used for several quasi-crimes. "Absolute liability" is used when the responsibility exists without fault, but the defendant is relieved of it by proving an external factor as the cause of the damage. This liability is based on no-fault for criminal acts and is never applied to non-criminal acts. It is only used for activities that are legal but dangerous, like those that "Responsibilite Pour Risque" is applied in written law without any breach of duty being required. It should be noted that absolute liability is described with different terms, including Liability without Fault (responsabilité sans faute), Presumed Responsibility, Objective Liability (responsabilité objective), and Risk Liability (responsabilité pour risqué crée). For the first time, absolute liability for environmental pollution was foreseen in the " Comprehensive Environmental Response, Compensation and Liability Act (CERCLA) (1980) in the United States, and the American states adopted it regarding the release.

Dangerous substances were accepted into nature. Although the historical root of absolute liability in common law goes back to the responsibility against the damages caused by animals and the employer's responsibility towards the workers, gradually, it was accepted for activities with unusual risks and environmental pollution. Absolute or no-fault liability is a new definition in civil liability law as well as modern criminal law. In short, absolute civil liability is a kind of civil (or criminal) liability that does not require psychological proof where the mere act of material behavior constituted by a crime/violation causes civil liability. Therefore, this type of responsibility is completely related to crimes with no need for proof of a psychological element.

These violations, also called material or absolute violations, it is thought that the perpetrator can be imposed by a guarantee of execution, including punishment, by simply performing a material act. This is justified by the close relationship between the psychological element and the material element with absolute liability. In the common law, it is supposed that crimes with absolute liability may be committed without any psychological element and by performing only an aspect of the material element14.

1. The tendency of the legal system of Iran and the European Union towards absoluteness of civil liability for environmental damages

In Iran, there is no clear sign of accepting this approach in the environmental legislation process. In some countries, the absolute nature of environmental crimes has eliminated the burden of verifying the psychological element in environmental crimes and made the legal and judicial confrontation with these crimes easier. Instead, these changes have put the duty to prove the lack of psychological element has been placed on the defendant's shoulder. But in Iran, the judicial authority is still obliged to prove

the psychological element of such crimes along with the other two elements, i.e. legal and material, to establish criminal liability and the possibility of applying the guarantee of legal enforcement against environmental crimes. It seems that such an approach is not rational in any way and is in clear conflict with the new criteria in the field of criminal liability resulting from the commission of environmental crimes. However, accepting no need to prove the psychological element in environmental crimes and confining it to committing criminal behavior, on the one hand, frees the judicial authority from the difficulties of proving the crime's psychological element, and on the other hand, makes it easier to prove the occurrence of the crime. It also enforces the preventive mode of relevant laws because everyone will know that should be more careful about environmental damage. The sensitivity to the environment increases to an extent that even without the need to prove the psychological element, any type of harmful behavior toward the environment will be a crime, and the perpetrators will be held criminally responsible.

The lack of need to prove the psychological element in environmental crimes will be doubly important when it is understood that in the modern world, usually many environmental crimes are carried out in a corporate (participatory) manner and sometimes by legal entities while accepting the "principle of differentiation in punishing environmental crimes", manifested by the lack of need to establish the psychological element, problems caused by the need to prove a psychological element in the criminal behavior of legal entities or in the assumption of committing a crime cooperatively will be eliminated. On the other hand, a problem in Iranian's laws for compensating environmental damages (regardless of whether these damages directly caused harm to people or whether they only target the environment) is the lack of a proper basis for the government's civil liability, because usually, the courts condemn environmental polluters to compensation based on the laws established on the theory of fault. This is even though this theory leads to many problems in environmental issues because it is very difficult to prove the fault of the polluter and when the environmental pollution has direct victims, their motivation to file a lawsuit and claim damages will be reduced. This difficulty is doubled when the government is the cause of the loss, because the structure of the government consists of employees whose actions may cause a lot of damage to the environment without being related to the government apparatus, as a result of the loss in the maze of proving the causal relationship between The act or omission of the cause of the loss and the damage caused, and then proving the fault of the cause of the loss, will be caught and maybe discouraged from filing such a lawsuit[15].

In the European Union, the approach of the legal system of England is mentioned, which is one of the most important legal systems in the world today, which focuses on the absolutism of environmentally damaging behaviors. The approach of the English legal system, in this case, can be examined especially for environmental crimes, but the point is that for harmful behaviors as well as environmental crimes, the principles emphasized by jurists regarding the absoluteness of liability have followed the same path

and no difference exists in this respect between theoretical foundations and approaches. A clear example is the tendency to omit the need to prove the intentionality of environmental crimes, and instead, let the judicial authority verify this intention in the committed behavior and accept no-fault liability (purely material) or, in other words, absolute liability in environmental crimes. England seems to be the first legal system in which the tendency to accept criminal liability without fault, or based on committing a material element, without considering the psychological element has beenformed16.

3. Developments in demonstrative evidence of civil liability for environmental damages

The evolution in the evidence system regarding complaints of civil liability for environmental damages should be studied based on the belief in absolute liability, and regarding it as the basis for environmental damages. Since absolute liability is the basis for the realization of civil liability for environmental damages, the demonstrative evidence for liability also becomes distinctly different from what is commonly proposed.This development is caused by the belief in the absoluteness of liability. In the transformation of the basis of civil liability from fault to absoluteness, the way of presenting evidence to prove complaints also changes significantly, while if the civil liability is based on fault, the demonstrative evidence is mainly the confession of the defendant to what he has committed. If absolute civil liability is realized, the demonstrative evidence is mainly based on the committed behavior. In other words, if the civil liability is based on fault, the priority of proving complaints is the defendant's confession of his harmful behavior. Therefore, if the defendant does not admit to what caused the damage, it will be difficult to prove the damage complaint on his part.

On the contrary, if the basis for realizing the civil liability is not the fault of the defendant, but merely the commission of a harmful behavior, the commission of the behavior is enough to prove his liability. In this assumption, even if the defendant did not admit to his behavior, his liability can be considered realized by referring to the evidence and circumstances related to his behavior. Therefore, the defendant's lack of confession is not an obstacle to proving the civil liability against the defendant, because by referring to the peripheral condition of the committed behavior, his civil responsibility is easily proven[17].

Basically, in the transformation from no-fault liability to absolute liability, one should know that the industrial revolution in the 19th century weakened the appeal of the theory of fault because the new production systems caused losses to workers and consumers, proving the fault of the damage caused was difficult. Accidents caused by transportation and worker-employer relations in the industry further showed the weakness of the theory of fault, and gradually the social theory of rights was proposed, which denied the involvement of intent and fault in the occurrence of damage, and emphasized that rights have social goals that should be reached. Jusran, the theory developer, believed that the theory of fault was not fair while justice dictates that the person who has caused the damage must compensate for

it even if no fault has been committed, instead of imposing the damage on a suffered person someone with no role[18]. Following these criticisms, the French jurist, Sally, also considered a criminal liability to be separate from civil liability and denied the involvement of the moral and fault in causing damage. Therefore, Reaper opined that due to the shortcomings of the theory of fault, its followers gradually moved to a theory similar to the theory of risk. In this regard, the insistence of the courts on the labor contract between the worker and the employer could be referred which considered the guarantee of the worker's health as the result of the implicit contract of work, and the provision of the passenger's health in the transport contract as the result of the implicit obligation for the benefit of the third party, to prevent damages to workers and passengers.[19]

Examining the basics of liability in law shows that a noted development in civil liability in terms of explaining, diagnosing, and determining the basis of civil liability for environmental damages is a thematic (or objective) liability while the fault has no place, and what matters is establishing the causal relationship between the act/omission of an act and the damage. Many legal developments around the world regarding demonstrative evidence systems for civil liability for environmental damages also tend towards absolute liability to the extent that even the most loyal professors following the theory of fault state that "although it is not the case today, soon it will turn out that most damages are compensated through strict liability and this theory governs the principle of fault" Some jurists have spoken about bringing civil liability closer to criminal liability. Several approaches focusing on the unquestionable importance of the environment, its easy access, and its critical role in human life deem that environmental crimes have a completely anti-human nature, and the principle of criminal strictness against these trespassers perpetrators has been the top priority of legislators in some countries. One of the most prominent manifestations of this strictness is seen in identifying the psychological element of environmental crimes. Air polluting behaviors are also an important manifestation of environmental crimes[20].

Environmental crimes could be examined from various legal angles, including a psychological perspective. Analyzing the psychological element of environmental crimes includes crustal material raised in environmental criminal law and is different from the normal procedure of studies in criminal law. Therefore, it could be analyzed as interdisciplinary by both environmental law and criminal law.Regarding diagnosis, determination, and explanation of civil liability for environmental damages, the criterion of fault theory is used in Iranian law, and seemingly, even though many professors and theorists believe in the establishment of civil liability for environmental damages, the Iranian legal system is far from assuming this type of liability. More precisely, many theorists of civil liability for environmental damages believe that the environment is the basis of life and the formation of human society; As a result, protecting it is the duty of all human generations. Today's man has more responsibility in this field due to the excessive use of resources.

Law, as the official system that shapes human relations, must fulfill its duty in protecting the environment well. For this purpose, solutions have been designed in different branches of law, including public law and private law. Public law by determining the international responsibilities of governments and organizational responsibilities, and private law by specifying civil responsibility do their duty in this case. Civil liability is a tool of private law to protect the property and financial rights of individuals and to compensate for the losses incurred. In civil liability, the damage must be compensated based on traditional principles. The basic elements of civil liability are damage, harmful act, and the causal relationship between the previous two elements. However, due to the specific nature of environmental damages, it is possible that traditional civil liability and its principles be insufficient to meet the goals of civil liability. Therefore, civil liability can improve this role by developing special solutions not specific to environmental damages. These solutions mainly consist of the wider use of no-fault or absolute liability and tolerance in proving the causal relationship. These cause civil liability to play a decisive role in compensating environmental damages and at the same time preventing such damages from occurring[21].

The legislation system regarding the environment includes principles, regulations, and instructions that must be observed not only by the EU institutions and both real and legal members but also should be considered in all the policies of the EU. Therefore, the regulations of liability arising from the violation of these laws are also very comprehensive and strict. In this type of liability, it is assumed that no-fault liability better ensures the implementation of the EU policies and principles for environmental protection.Seemingly, the main legal document available at the European Union to establish the system of civil liability for environmental damages based on the criterion of absolute liability is the Directive of the European Parliament, 2004, which believes in the realization of civil liability for environmental damages based on environmental liability or civil liability without fault. In this directive, the mere fact that the damage is imminent is considered sufficient to file a claim and the potential damage is allowed to take preventive measures. Another necessary condition for claiming damage is that the direction should be direct. Of course, this condition is more related to verifying the causal relationship between the damage and the person's act, than to the conditions of claimable damage.

The meaning of the condition of direct damage does not mean that no other cause is involved in the occurrence of the damage, but rather it refers to establishing a customary causal relationship. Therefore, when the wind releases the polluting substances of a factory into the air and the villagers suffer from respiratory disease, the usual reference of damage belongs to the factory, and the factory cannot be exempted from paying damages due to the wind. Another condition for proving direct is the ability to predict it based on its nature, not the amount. Regarding the environmental damages liability, based on the following philosophy, this condition should be doubted or at least limited to cases where the polluter was not at fault or negligent in not foreseeing the damage, because, for example, exempting

a hospital that discharges its sewage into the city river and makes some people ill, simply because the hospital officials could not predict the damage, is against legal justice and the goal of environmental protection[22].

The most important principle accepted by the European Union based on the belief in absolute civil liability for explaining environmental damages is the "Payment by the polluter", which shapes the basis for the complaints proof system. This principle is determined by the Organization for Economic Cooperation and Development (OECD). This principle refers to the allocation of costs to prevent pollution, established as a control regulation by public authorities, and encourages the members of the European region to use rare environmental resources properly.Following the changes that occurred in the evidence system regarding civil liability complaints caused by environmental damages, the proof system of these complaints has also evolved. No need for confession in for proving complaints as well as the emphasis on the importance of other proofs, especially in the UAE Legal and judicial proving these complaints are among the most important changes. As much as the judicial authority is disappointed by the action of the defendant to confess an environmentally damaging behavior, he can attend to other evidence, including certificates and legal and judicial presumptions.

Therefore, there is no need for the defendant's confession for committing an environmentally damaging behavior; it can be proved based on testimony and evidence of committing, or by referring to legal and judicial presumptions. This is a prominent change in the demonstrative evidence of civil liability for environmental damages since omits the need to obtain the defendant's confession to prove these complaints only with the help of other evidence. However, the foundation of the civil liability system and proof of liability based on fault in Iran's legal system greatly limits the ability of judges and judicial authorities to transform this system.

Despite many lawyers' efforts to convince the legislator and official authorities to accept absolute liability in the field of realizing civil liability for environmental damages, no positive development has occurred in this field in Iran's legal system. The two judicial rulings mentioned before confirm that Iran's legal system is facing a dilemma in changing traditional principles of civil liability caused for environmental damages. While recognizing and accepting the basis of absolute liability, in practice, will help the judicial authorities in easily affirming the liability and guarantee caused

by environmentally damaging behaviors. The weakness of Iran's legal system in this field is evident while some jurists, referring to several jurisprudence principles including "no harm and loss", believe that in the Islamic legal system, contrary to the notions, the absolutism of civil liability for environmental damages not only existed before but at least these two important rules could be the basis for the official and legal identification of absolute liability for environmental damages in Iran[23].

Close analysis of the European Union's approach to evolution in the system of proving complaints of civil liability for environmental damages reveals important points. Discussions about the expansion of

the environmental liability regime in the European Union are very controversial since the tendency towards environmental liability differs in each specific member. These issues often arise from policies related to environmental incidents. The first action for describing the regime of civil liability for environmental damages in the European Union dates back to the Directive on the care and control of hazardous waste transport by ship, 1984. The first activities were limited to the establishment of a liability regime for damages caused by sewage, which the European Commission presented in 1989 with a proposed directive on civil liability for damages caused by sewage. But this proposal was canceled in 1993 when the commission thought of a broader liability regime. The first high-level goals of the commission are related to the statement of its positions known as the Green Paper on Environmental Liability in 1993, which was written about compensation for environmental damages. This new measure was implemented in the Union at the same time as the signing of the Convention on civil liability for damage resulting from activities dangerous to the environment (Lugano), 1993. This convention is supported by the Council of Europe, which currently has more than 44 members. That is, almost all the countries of the European continent are participating in its discussions, but only 9 countries signed it (Cyprus, Finland, Greece, Iceland, Liechtenstein, Luxembourg, Netherlands, and Portugal).Conclusion

Protecting the environment is so important that the classical international liability based on the commission of a wrongful act is now shaken, and the strict liability - which only requires proof of the occurrence of harm, the occurrence of a harmful act, and the causal relationship between the harmful act and the damage caused to the environment, - in government activities, judicial procedure, and international arbitration, international documents and even domestic laws have been emphasized. The International Law Commission, by raising the international responsibility resulting from acts not prohibited in international law, through the approval of two draft articles of 2001 on "prevention of transboundary damage caused by risky acts" and the draft principles of 2006 "allocation of damages in damage transboundary due to risky actions", has taken a further step in protecting the environment. It should be noted that the nature of this liability requires that, unlike the responsibility of governments for internationally wrongful acts, there is no longer a need for " full reparation " and "adequate compensation" should be replaced since this type of liability arises from the legal activity and In compensation, it is not necessary to erase all the effects of that activity.

The basic approach of the international liability system to environmental damages is preventive and it has shaped all the differences and approaches. In other words, the international liability law's view of environmental damages is preventive rather than curative. This roots in the vast and some cases, irreparable nature of environmental damages. This preventive approach is manifested in two ways in this type of liability: the development of primary rules through secondary rules, and the acceptance of absolute liability for the operator.

Regarding the development of the primary rules through the secondary rules it should be mentioned that in the liability resulting from non-prohibited actions, the primary rules have been formed based on the secondary rules because prevention is essentially focused on the stage before the secondary rules, and these rules are not included in the prevention filed.

Based on this, the International Law Commission has revised the rules of responsibility for non-prohibited acts by following the basic rules, that is, the 2001 articles of the International Law Commission on "prevention of transboundary damage caused by risky acts" and the 2006 principles of the Commission on "allocation of loss in a cross-border damage caused by risky acts".Regarding accepting absolute liability for the beneficiary, imposing absolute heavy responsibility seems a good motivation for him to avoid damages in the future because he assesses the state of the legal rules governing the responsibility for prohibited acts and finds the most economical way to prevent the occurrence of environmental damages as much as possible. So apparently the best way to protect the environment is to prevent damage. In this regard, the International Law Commission has taken an effective step in adopting a preventive approach through the acceptance of absolute liability for the perpetrators of risky acts not prohibited in international law in the 2006 draft of principles regarding "allocation of loss in cross-border damage caused by risky acts ".

The second approach focusing on the responsibility for non-prohibited actions is privatizing liability. In other words, according to the rules of classical international liability, that is, responsibility for internationally wrongful acts, liability is raised at the state level, but in the case of international liability resulting from non-prohibited acts, the responsibility is not only raised at the state level but manifested with a private approach. The approach of privatizing liability in non-prohibited actions has been achieved in two ways: by accepting the initial liability of the beneficiary instead of the responsibility of the government of origin, which is also referred to as channeling the liability towards the beneficiary, and by reducing liability from the intergovernmental level to the internal rights of the government of origin.

The last approach is collective liability. In other words, the liability resulting from risky but not prohibited actions is first imposed on the operator, meaning that he is the one who should compensate for the damage caused, and the government of origin has the duty to, first, guarantee immediate and adequate compensation for the damage by the operator, and secondly, if it is not possible to collect compensation from the operator for any reason, the government will compensate the damage.As manifested, the questions raised in this research are answered and the hypotheses are proven. In other words, the first hypothesis, regarding changes in the approach of the international liability system towards transboundary damages for dangerous activities (acts not prohibited in international law), especially environmental damages, and the second hypothesis, i.e, the international liability system has been changed regarding prevention of environmental damages, privatization of international liability

and collective liability in environmental damages were investigated and proven.Iran's laws are far from what is going on at the level of the European Union to recognize this important feature of the rules of civil liability for environmental damages. The Iranian legislator is expected to pay attention to this phenomenon in the current situation. Also, the judicial procedure can insist less on the necessity of the principle of individualization of penalties and should compensate more environmental damages by attending to the changes made in the rules of civil liability for environmental damages in the contemporary legal literature around the world.

On the other hand, discussion about the international responsibility of governments for damages to the environment and its components is a new issue that has attracted the attention of the international community, and signs of it can also be found in the sources of international law. Of course, the occurrence of this responsibility depends on the transboundary nature of many environmental damages, which have affected the international community. Although civil liability is a domestic issue, damages are not limited to domestic borders at the environmental level (e.g., pollution caused by nuclear accidents). For this reason, it may have a transnational aspect. A critical issue in this field is determining the person responsible for compensation.

Although at the level of legal doctrine various analyzes and research have been performed and specific proposals have been explicitly suggested to identify both cases in the legal system of civil liability for environmental damages by domestic policymakers, no outstanding changes have occurred in Iran's legal system, while it seems that civil liability for environmental damages is in dire need of both transformations in the nature.

REFERENCES

1. Babaei-Moghadam, Abedin, Examining the Differences between Environmental damages and other Damages and the Effects of a Differential View in the Field of Personal Liability, Master's Thesis in Environmental Law, Shahid Beheshti University, 2013, p. 45.

2. Bahrami Ahmadi, Hamid and Azizullah Fahimi, The Basis of Environmental Civil Liability in Iranian Jurisprudence and Law. Journal of Islamic Law Research, 8 (26), 2016, p. 134.

3. Bahrami Ahmadi, Hamid and Azizullah Fahimi, The Basis of Environmental Civil Liability in Iranian Jurisprudence and Law, Journal of Islamic Law Research, p. 137.

4. Dabiri, Farhad et al., Investigating Compensation for Environmental damages Caused by Transboundary Pollution and International Environmental Destruction, Journal of Human and Environment, 12, 2019, p. 51.

5. Doroodian, Hassan Ali, Civil Laws 4, Civil Liability Laws, Lectures of the Bachelor of Judicial Law, Faculty of Law and Political Sciences, University of Tehran, 2017, p. 83.

6. Draft Principles on the Allocation ..., op. cit., p. 127, para. 11.

7. Fahimi, Mustafa, Environmental Criminal Law, Khorsandi Publications, First edition, 2017, pp. 98; And Taghizadeh Ansari, Mustafa, Environmental Criminal Law, Borna Publications, First edition, 2013, pp. 128-141.

8. Gardner, John, Answering for Crime, Responsibility and Liability in the Criminal Law, Hart Publishing, R A- Duff, 2007 , p. 113.

9. Hayward, Tim, Constitutional Environmental Rights, Oxford University Press, USA, 2005 , p. 5.

10. J.P.H Trevor(1969) Principles of Civil Liability for Nuclear Damage, in: Nuclear Law for a Developing World, Legal Series, No.5,

IAEA, Vienna, p. 109; Liability and Compensation for Nuclear Damage, first edition, NEA/ OECD, Vienna, 1994, p.16.

11. Jan Schnieder, World Public order of the Environment: Towards an International Ecological Law and Organization, University of Toronto Press, Toronto, 2009, p. 168.

12. Katouzian, Nasser, Civil Rights (Compulsory Warranty), First volume, Tehran University Press, 19th edition, 2017, p. 243.

13. Leila Amini, "International Responsibility of Governments due to Environmental Pollution", Master's thesis, Faculty of Law, Shahid Beheshti University, 2019, pp. 26-27.

14. M. B. Akehurst, International Liability for Injurious Consequences Arising out of Acts Not Prohibited by International Law, NYIL., 2003, p. 3.

15. Majnounian, Henrik, Global Strategies and Treaties for the Protection of Nature and Living Resources, Journal of Environmental Protection Publications, 9th edition, 2009, p. 271.

16. Mirhosseini, Seyyed Majid and Farsima Khamsipour, Law Governing Civil Liability Claims Due to Environmental Destruction in European Union and Iranian Law, Journal of Strategy, 73, 2013, p. 114.

17. Mohsen Zadeh, Ahmad Ali and others, Environmental Law; Theories and Procedures, Publications of Environmental Protection Organization, second edition, 2010, p.51.

18. Nowroznia, Roya, Investigation of Civil Liability Caused by Pollution and Damage to the Environment in Iran's Thematic Law and International Conventions, Master's Thesis in Private law, Islamic Azad University, Garmi Branch, 2015, p. 112.

19. Qasimzadeh, Morteza, Civil liability due to omission, Judiciary Law Journal, No. 44, 2018, p. 51.

20. Ra'ai, Massoud, Fault in civil Liability and Justice, Journal of Legal Knowledge, 1, 2018, p. 173.

21. Raisi, Leila, International Liability Developments due to Environmental Samages according to the Basel Convention, Journal of Man and Environment, 13, 2019, p. 83.

22. Taghrangar, Hassan et al., Researching the Psychological Element in Crimes with Absolute Liability, Journal of Legal Research, N. 43, 2019, p. 75.

23. Vafadar, Ali, Commitment and Responsibility of Governments in Environmental Protection, Journal of Environmental Sciences and Technology, Volume 9, Number 1, 2005, p.59.

24. Wild, Mark L., The Ec Commission's white paper on Environment Liability: Issues and Implication, Journal of Environmental Law, Vol. 13, No. 1, 2001, p. 27.

ISSN: Print -0976-9234

Effect Of Maternal Anemia On Cord Blood Hemoglobin Of Full-Term Newborn

Parisa Zarif Najafi1, Yeganeh Mobasser2, Elaheh Mobasser3, Nahid Mobasser 4
1Department of Obstetrics and Gynecology, Islamic Azad university of medical sciences of Mashhad branch, Mashhad, Iran.2Department of Cardiology, Mashhad university of medical sciences, Mashhad, Iran.3Department of Obstetrics and Gynecology, Razavi Hospital, Mashhad, Iran.4Department of Cardiology, Zanjan university of medical sciences, Zanjan, Iran.Correspondence: Yeganeh Mobasser.
Email: yeganehmobasser4257@gmail.comDOI: 10.47750/pnr.2022.13.04.271

A B S T R A C T

Background and purpose: Anemia during pregnancy is related to major problems of mother and fetus. The purpose of the study was to find any correlation between maternal anemia and the baby's cord blood hemoglobin (Hb) level.

Methods: This cross-sectional study was conducted in neonatal and midwifery departments women in Mashhad Azad University hospitals from January 2014 to September 2021.A total of 200 pregnant women over 34 weeks of pregnancy who gave birth participated in the study and umbilical cord blood. The hemoglobin of their babies was collected. Average maternal hemoglobin and average cord blood hemoglobin comparison using Pearson's correlation coefficient in different non-anemic, anemic, mild, moderate, and severe anemia groups were classified.

Findings: Out of 200 pregnant women, 136 (67.8%) were anemic and 64 (32.2%) were not anemic. Medium hemoglobin in non-anemic mothers and anemic mothers was 11.67 and 9.56 g/dl, respectively. Pearson's correlation coefficient of non anemic, anemic, mild, moderate, and severe anemia groups with $P<0.05$ is statistically significant, which showed a positive correlation between maternal hemoglobin and umbilical cord hemoglobin.

Conclusion: From this study, we concluded that maternal anemia affects the hemoglobin of the baby's umbilical cord blood. According to the findings, anemic women give birth to babies with lower hemoglobin levels than non-anemic mothers. Findings showed a linear relationship between maternal hemoglobin and cord blood hemoglobin of their babies.

Keywords: Anemia, Pregnancy, Hemoglobin

INTRODUCTION:

Anemia is very common during pregnancy in developing countries. According to WHO/World Health Statistics data, 40.1% of pregnant women worldwide were anemic in 2016. The problem is particularly common in Asian countries, where anemia is responsible for about half of maternal deaths. Worldwide, more than 300,000 women die each year due to complications during pregnancy and childbirth. The World Health Organization (WHO) reports that around 700 women die each year in the United States, with approximately 830 women dying each day worldwide. Most of these women (99%) live in poor and developing countries. In some places, the chance of dying from pregnancy is as high as 1 in 15. The

sad reality is that many of these deaths are preventable. (1).Cord blood hemoglobin is an essential predictor of anemia in newborns at delivery. It used to be assumed that the baby would not be anemic regardless of the mother's hemoglobin level. According to several studies, women who had iron deficiency anemia during pregnancy gave birth to babies with reduced hemoglobin levels in the cord blood. Recent research has discovered a linear relationship between the mother's hemoglobin and the baby's umbilical cord blood hemoglobin. Cord blood for newborn lab tests is a promising new method that has been found to improve newborn outcomes. As a result, the full implementation of this method is a vital step towards improving the use of cord blood in improving neonatal outcomes (2).Further research is needed for important validation the relationship between maternal hemoglobin level and the umbilical cord of the newborn the aim of the study was to see how the Hb level of the blood maternal Hb anemia affected the baby's umbilical cord blood.

This cross-sectional study in the sector pediatrics and Obstetrics Azad University hospitals in Mashhad from January 2014 to September in 2021. All pregnant women over 34 weeks of pregnancy and their babies were included in this study. Mothers with risk factors such as antepartum bleeding, blood pressure, gestational diabetes due to pregnancy, kidney disease, hypothyroidism and babies who have given birth to twins, asphyxia at birth, congenital and pathological abnormalities, jaundice such as Rh incompatibility, are excluded. A total of 200 pregnant women participated in the study, and cord blood Hb of their infants was collected after obtaining their informed consent. Maternal hemoglobin was tested before delivery and mothers were divided into two groups based on maternal hemoglobin levels. The anemia group was divided into mild (Hb 10-10.9 g/dL), moderate (7-9.9 g/dL) and severe anemia (Hb <7 g/dL). The data was analyzed using descriptive statistics using SPSS version 26 software. Pearson's correlation coefficient was used to find a linear correlation between maternal anemia and umbilical cord blood hemoglobin with a p value less than 0.05, which was considered statistically significant. The mean hemoglobin of mother and the mean hemoglobin of umbilical cord blood in non-anemic groups were compared using Pearson's correlation coefficient (R=0.67) and it had a positive and significant correlation with $p<0.001$. Similarly, Pearson correlation coefficient of mild, moderate, and severe anemia were 0.84, 0.65, 0.72 respectively with $P<0.05$, which showed a positive correlation between maternal hemoglobin and cord hemoglobin (Table 1).

Discussion

The findings of our study were consistent with those of Klebanov et al. (1991) and Lu et al. (1991) who reported an association between maternal anemia and a higher risk of preterm birth. The research findings were present (3).

Like the study conducted by Prasad et al. who reported a positive and significant relationship with the increase in the number of children and pregnancy status. Our findings were comparable to those of Tembhare et al who found the number of vaginal deliveries, instrumental deliveries, and caesarean section. Sections (LSCS) were similar in both anemic and non-anemic mothers, but more anemic mothers required labor induction. Our findings were consistent with them (4,5,6).Figueiredo et al found that maternal anemia was associated with low/inadequate birth weight, suggesting that it is a risk factor for pregnancy outcomes assessed (7).

The present study compared maternal hemoglobin with infant cord hemoglobin to see if there was a correlation between the two measurements. As the mean hemoglobin of the mother decreased, the mean hemoglobin of the umbilical cord also decreased, which indicated a linear correlation between the hemoglobin of the umbilical cord and the mother's hemoglobin. This suggests that maternal anemia influences cord Hb. This indicates that at higher levels of anemia, placental iron is transferred mechanisms may fail, resulting in decreased umbilical cord Hb (8).The findings of our study were like the study conducted by Timilsina et al., which showed a moderate positive correlation between maternal and fetal hemoglobin.

Our findings were comparable to the study by Sarin et al., who concluded that infants born to anemic mothers had lower umbilical cord blood Hb than non-anemic mothers. Also, our findings were like a study conducted at Babol University by Najiba et al., which showed a linear relationship between maternal hemoglobin and infant cord hemoglobin. Debarma et al. found a linear relationship between umbilical cord and maternal hemoglobin, which is like the present study. In another study conducted by Mamoury et al. From northeastern Iran, contradictory findings were reported that there is no relationship between cord blood hemoglobin, umbilical cord hemoglobin, or maternal hemoglobin (9,10,11).

Conclusion

This study concluded that maternal anemia affects the hemoglobin of the infant's cord. Based on findings, anemic mothers give birth to babies with lower hemoglobin levels than non-anemic mothers. The findings show that there is a linear correlation between the mother's hemoglobin and the hemoglobin of the cord blood of their babies. Prevention during pregnancy may prevent anemia in underdeveloped countries such as Iran, perhaps reducing the risk of fetal and maternal problems and thus improving infant survival rates.

Table 1: Relationship between maternal hemoglobin (Hb) (g/dl) and cord Hb (g/dl) in pregnant women (N=200).

Pregnant women Hb	N	Mean maternal	Mean cord Hb	Pearson correlation coefficient	P value
		Hb			
Non-anemic (Hb≥11)	64	11.67	17.02 (1.36)	0.67	
Anemic (Hb<11)	136	9.56	15.56 (0.57)	0.71	<0.001
Mild anemic (Hb 10-10.9)	59	10.43 (0.18)	15.28 (0.87)	0.84	<0.001
Moderate anemic (Hb 7-9.9)	60	8.68 (0.89)	15.16 (0.44)	0.65	<0.001
Severe anemic (Hb	17	6.43 (0.82)	14.43 (0.53)	0.72	<0.001

REFERENCES

1. Maternal mortality, 2019. Available at: https://www.who.int/news-room/fact-sheets/detail/mate.

2. Jung J, Rahman MM, Rahman MS, Swe KT, Islam MR, Rahman MO, et al. Effects of hemoglobin levels during pregnancy on adverse maternal and infant outcomes: a systematic review and meta-analysis. Ann N Y Acad Sci. 2019;1450(1):69-82

3. WHO. Hemoglobin concentrations for the diagnosis of anemia and assessment of severity. Vitamin and Mineral Nutrition Information System, 2011. Available at: https://www.who.int/vmnis/indicators/haemoglobin.pdf. Accessed on 05 December 2021.

4. Breymann C, Bian XM, Capito LR, Chong C, Mahmud G, Rehman R. Expert recommendations for the diagnosis and treatment of iron-deficiency anemia during pregnancy and the postpartum period in the Asia-Pacific region. J Perinat Med. 2011;39(2):113-21.

5. Shukla AK, Srivastava S, Verma G. Effect of maternal anemia on the status of iron stores in infants: A cohort study. J Family Community Med. 2019;26(2):118-22.

6. Bernhardt GV, Jhancy M, Shivappa P, Bernhardt K, Pinto JR. Relationship between Maternal and Cord Blood Iron Status in Women and their New Born Pairs. Biomedical and Pharmacol J. 2021;14(1):317-23.

7. Kohli UA, Rajput M, Venkatesan S. Association of maternal hemoglobin and iron stores with neonatal hemoglobin and iron stores. Med J Armed Forces India. 2021;77(2):158-64

8. Kant S, Kaur R, Goel AD, Malhotra S, Haldar P, Kumar R. Anemia at the time of delivery and its association with pregnancy outcomes: A study from a secondary care hospital in Haryana, India. Indian J Public Health. 2018;62(4):315-8.

9. Figueiredo ACMG, Filho IS, Batista JET, Orrico GS, Porto ECL, Cruz PRM, et al. Maternal anemia and birth weight: A prospective cohort study. PLoS One. 2019;14(3):212817.

10. Sareen A, Singh S, Mahajan K. Maternal Anemia and its Effect on Cord Hemoglobin. Paediatr Rev Int J Paediatr Res. 2018;5(7):351-4.

11. Mamoury GH, Hamedy AB, Akhlaghi F. Cord hemoglobin in newborns in correlation with maternal hemoglobin in northeastern Iran. Iranian J Med Sci. 2015;28(4):166-8.

ISSN: Print -0976-9234

Comparing Thyroid Biomarkers And The Quality Of Nuclear Scan Images Of Patients With Thyroid Cancer After Levothyroxine Withdrawal Or Receiving Thyrotropin Alfa: A Retrospective Study

Sara Kavousi1, Forouzan Ahmadpour2*, Mohammad Hossein Emdad3, Farshid Gheissari4

1Pharmacy student, Lorestan School of Pharmacy, Lorestan, Iran, Email: ara.k1373@yahoo.com, ORCID: 0000-0001-9036-28462*Assistant professor of clinical pharmacy, Razi Herbal Medicines Research Center, School of Pharmacy, Lorestan University of Medical Sciences, Khorramabad, Iran, Email: ahmadpourforoz@yahoo.com, ORCID: 0000-0002-1142-60883General Practitioner, Shiraz University of Medical Sciences, Email: aminm685@gmail.com, ORCID: 0000-0002-4999-8620 4Assistant Professor and Nuclear Medicine Specialist and Head of Nuclear Medicine Department, Shiraz University of Medical Sciences, Email: fgheisari@gmail.com, ORCID: 0000-0002-1113-3744

*Corresponding author: Forouzan Ahmadpour, Email: ahmadpourforoz@yahoo.com

DOI: 10.47750/pnr.2022.13.04.275

ABSTRACT

Background: Thyroid scan is a specialized imaging method for assessing thyroid cancer after thyroid gland removed. To prepare the patient before scanning the thyroid gland, levothyroxine withdrawal or injection of thyrotropin is done. The aim of the study: The present study aimed to evaluate the quality of nuclear scan images and thyroid biomarkers after levothyroxine withdrawal or receiving thyrotropin alfa. Materials and Methodology: This was a cross-sectional study. The statistical data of this research were composed of 80 female patients with thyroid cancer referred to the nuclear medicine department of the Namazi Hospital in Shiraz in 2019. To be eligible to participate in this study, the patients must have a history of thyroidectomy, a Body mass index (BMI) of between 26 and 30 kg/m2, and no history of receiving radioactive iodine uptake. To nucleus scan of the thyroid gland, all patients received 150 millicuries of radioactive iodine. Patients were divided into two groups. The first group consisted of 40 patients who had discontinued levothyroxine a few weeks before the nuclear scan. The group consisted of 40 patients who continued levothyroxine and received thyrotropin alfa (Thyrogen brand name) before the nuclear scan. These two groups were compared in terms of the levels of thyroid-stimulating hormone (TSH), Triiodothyronine (T3), thyroxine (T4), and thyroglobulin (Tg) biomarkers and image quality following the opinion of nuclear medicine experts and the Region of Interest (ROI) criterion. The results: There was no statistically significant difference between the two groups in T3 and T4 levels. In contrast, the mean TSH level was 67.37±13.98 mIU/L in patients with thyroid hormone withdrawal (THW) and 72.90±16.50 mIU/L in patients who had received thyrotropin alfa injections (P<0.001). The mean Tg levels in the THW and thyrotropin alfa injection were 244.58±88.48 mIU/L and 198.40±61.76 mIU/L, respectively (P<0.001). The means of the body count parameter in the THW and thyrotropin alfa injection groups were 37629.28±9817.08 m2and 21165.25±3346.64 m2(P <0.001), respectively. Based on the comments of nuclear medicine physicians, the high qualities of the images were 27.5% and 65% in patients with THW and who had

been injected with thyrotropin alfa, respectively. Discussion and Conclusion: The TSH biomarker was higher in patients who had gotten thyrotropin alfa injections, which prepared these patients for the thyroid nucleus scan without the patient's developing symptoms of hypothyroidism. Tg levels were higher in patients with THW, suggesting the likelihood of recurrence of disease, metastasis, and/or residual thyroid tissue in this group. The body count parameter was higher in patients with THW, indicating lower image quality in this group than in the group receiving thyrotropin alfa injections. Besides, the image quality was better in the thyrotropin alfa injections group. Therefore, according to the results of this study, receiving thyrotropin alfa injections was preferable to discontinuation oflevothyroxine.

Keywords: Thyroxine, Thyroglobulin, Thyroid Cancer, Radionuclide Imaging, Thyrotropin AlfaIntroduction

INTRODUCTION

Thyroid cancer is one of the most common endocrine cancers, which has become more prevalent in recent decades (1). According to a study by the National Cancer Institute in 2019, about 52890 people in the United States developed thyroid cancer. Also, approximately 70% of these people needed a thyroid scan, and 40% needed a thyrotropin alfa injection (2). Thyroid-stimulating hormone (TSH) is secreted by the anterior pituitary gland cells and plays a pivotal role in controlling thyroid function. It is also the most useful physiological indicator of thyroid hormone activity. Besides, TSH is the main factor determining the point of regulation in the thyroid axis.. The thyroid gland produces a hormone called triiodothyronine, known as T3. It also produces another hormone called thyroxine, known as T4. Together, these hormones regulate body temperature, metabolism, and heart rate (3-6). Iodine-131 (I131) is an essential radioisotope that is widely used in thyroid disease. This radioisotope is used to remove the remnants of cancerous tissues after thyroidectomy. Also, flat-field imaging, which is the most popular method for determining the level of radioactive I131 activity, is considered to identify metastatic diseases or cancerous tissues left in the thyroid gland after thyroidectomy (7). Two methods are commonly employed to prepare patients for a thyroid scan, i.e., thyroid hormone withdrawal (THW) or injection of thyrotropin alfa. After removing the thyroid gland (thyroidectomy), thyroid hormones should be replaced to avoid hypothyroidism symptoms and suppress thyroid cancer after thyroidectomy (8). The thyroid hormone cessation some weeks before scanning has long been used to prepare the patient for a nuclear scan. THW aims to increase the TSH level to enhance the uptake of radioactive iodine by healthy or metastatic thyroid cells or thyroid cancer cells. Another method for patient preparation is the injection of thyrotropin alfa that is produced by DNA recombinant technology. The advantage of this method is that it prevents the symptoms of hypothyroidism caused by the withdrawal of the thyroid hormone (9). Tg levels rise due to thyroid cancer; thus, the Tg is used as a tumor marker.

In this method, the thyrotropin alfa is taken a few days before the scan, and there is no need to stop the levothyroxine to increase TSH levels (10, 11). Tg levels should be undetectable or very low after thyroid resection or after radioactive iodine treatment, provided the patient is taking thyroid hormone (levothyroxine) daily to prevent the increase of TSH.

However, if Tg is still detectable in the blood after thyroid resection, the remaining thyroid tissue may either be normal or cancerous, which needs to be followed up and treated (12, 13). With the increasing use of radiotherapy medicine in clinics and animal trials, it is necessary to precisely assess the dose of the medicine absorbed by patients to assess the prognosis and side effects. Flat-field images taken by a gamma camera have been used to determine the condition and estimate the benignity or malignancy of a gland for decades. However, the difference between the estimated condition of the gland and its actual activity can be 4-6% to 10% or more for specific organs. This percentage is mainly determined by the definition of Region of Interest (ROI), context, distribution, and condition of the organ (12). To quantify flat-field imaging, the definition of ROI is a fundamental method that can affect the accuracy of quantitative results. However, studies quantifying thyroid radioactivity have not provided a consistent method for defining ROI (14). Most researchers have defined ROI based on visual specifications and depicted an area containing thyroid.

Nonetheless, a visual criterion is an ambiguous concept. In addition, several researchers have proposed other methods for determining target tissue of ROI, such as selecting an 85% isocount contour of the thyroid gland or considering system spatial resolution (15, 16). To sum up, the criterion for the ROI definition is an integrated target tissue and rarely have studied have been designed precisely and simply to use an ROI definition method. Recently, with the development of image data processing workstations, ROI and more precise contexts can be defined that enable the precise quantification of flat imaging (15). To put it differently, ROI is an image or a data set that is specified for a particular purpose. It includes a surface report of the body based on the square meter in which radioactive iodine is absorbed and is specified in the image (17). The amount of ROI is calculated by counting the areas that have absorbed radioactive iodine (in square meters). Body count signifies this amount in the relevant software. There is yet no quantitative study on the effect of thyrotropin alfa and THW on ROI and nuclear scan image quality and comparison between the two. Therefore, the present study aimed to evaluate the quality of nuclear scan images, and the level of thyroid biomarkers after discontinuing levothyroxine or receiving thyrotropin alfa and compare these two methods.

MATERIALS AND METHODS:

This study was a cross-sectional study that has been approved by the ethics committee of the Lorestan University of Medical Sciences (the ethics code number: IR.LUMS.REC.1399.173). For six months, researchers studied all medical records of patients with thyroid cancer referred to the nuclear medicine department of the Namazi Hospital in Shiraz to have a nuclear scan in 2019. A total of 150 cases was initially reviewed in six months. To participate in this research, the patients had to be females suffering from thyroid cancer who had undergone

thyroidectomy, had a Body mass index (BMI) of 26-30 kg/m2 , received radioactive iodine for the first time, did not have a history of iodine therapy, received a constant amount of 150 millicuries of radioactive iodine, did not suffer from other underlying diseases, and did not take any drug other than levothyroxine. Out of the 150 reviewed cases, 80 patients were selected and later divided into two groups. The first group consisted of 40 patients who had stopped taking levothyroxine for six weeks before their nuclear scan. The second group consisted of 40 patients who received thyrotropin alfa injections (in 2 separate injections 24 hours and 48 hours before receiving radioactive iodine), did not discontinue their levothyroxine intake, and were scanned. Laboratory thyroid factors, including TSH, T3, T4, and Tg were recorded just 24 hours after the thyrod scan for patients and compared our two groups together. To evaluate the imaging quality, researchers asked and recorded the opinions of three nuclear medicine experts. These people did not know which image belonged to which patient so that their judgment would not be influenced. Furthermore, to quantitatively compare the quality of images, the average ROI was recorded in each group and compared. Quantitative variables were evaluated as mean, standard deviation, minimum, and maximum. The normality of quantitative variables was assessed using the Kolmogorov-Smirnov test. Moreover, the two groups were compared in terms of quantitative variables using the independent t-test or the non-parametric Mann-Whitney test. A significance level of 0.05 was considered for the previously mentioned tests. Data analysis was performed using the Statistical Package for the Social Sciences (SPSS) software. Finally, Graphs were drawn in the GraphPad Prism software.

RESULTS:

The mean ages of patients with THW and patients receiving thyrotropin alfa injections were 51.4±14.94 and 54.00±8.95 years. Given P=0.35, there was no significant difference between the mean ages of the two groups. Also, the mean BMIs of patients in the THW and thyrotropin alfa groups were 27.27±1.39 kg/m2and 27.18±1.43 kg/m2, respectively. According to P=0.78, there was not a significant difference between the mean BMIs of the two groups. The Kolmogorov-Smirnov test was used separately for the groups to test the normality of the data. This test showed that the assumption of normal distribution of data did not apply to the variables TSH, T3, and T4 in the two groups. Therefore, the Mann-Whitney non-parametric test was used to compare the means of the variables. The mean T3 and T4 serum levels in patients with THW were 2.26±1.31 Ng/dl and 1.93±1.24 Ng/dl, respectively. The mean T3 and T4 serum levels in patients receiving thyrotropin alfa injections were 2.24±1.30 Ng/dl and 1.94±1.23 Ng/dl, respectively. Thus, according to P=0.67 and P=0.99, there was no significant difference between the mean levels of T3 and T4 between the two groups. The mean TSH and Tg levels in the THW group were 57.37±13.98 mIU/L and 244.58±88.43 mIU/L, respectively. The mean TSH and Tg levels in the thyrotropin alfa group were 72.9±16.50 mIU/L and 198.40±61.76,

Given P<0.001, there was a significant difference between the two groups in terms of the mean levels of TSH and Tg, in that the TSH of patients receiving thyrotropin alfa injections was significantly higher than the TSH in patients with THW. Figure 1 Also, the Tg of patients with THW was significantly higher than that of patients receiving thyrotropin alfa injections. Figure 2. The mean ROI parameters in patients with THW and patients receiving thyrotropin alfa injections were 37629.28±9817.08 m^2 and 21165.25±3346.64 m^2, respectively. Based on P<0.001, there was a significant difference between the mean body count level of the two groups, in that the ROI of patients with THW was significantly higher than patients who had received a thyrotropin alfa injection. Figure 3. The Chi-square test and descriptive information were used to determine the frequency of the variables and compare the variable of image quality in the two groups. The results suggested that 3 patients receiving thyrotropin alfa injections (7.5%) and 13 patients with THW (32.5%) had poor image quality. Besides, 26 patients receiving a thyrotropin alfa injection (65%) and 11 patients who had stopped levothyroxine (27.5%) had good image quality. Therefore, according to P=0.001, there was a significant difference between the two groups as far as image quality was concerned. Also, the Kramer correlation coefficient value, which is used to express the degree of correlation between two nominal and ordinal variables, was 0.41, which suggested a moderate correlation value.

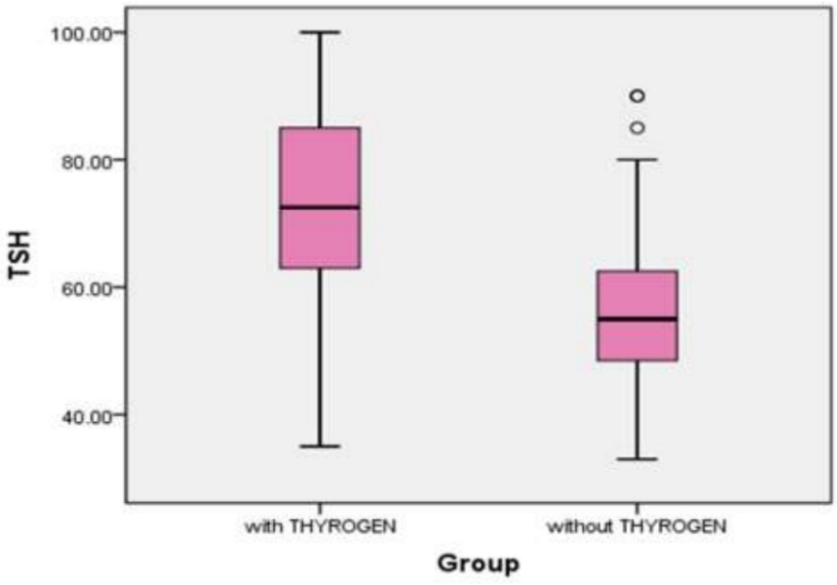


Figure 1: Comparing blood levels of TSH in the two groups using box plots. *TSH level is significantly higher in the patients who receiving thyrotropin alfa than the patients who had stopped levothyroxine.

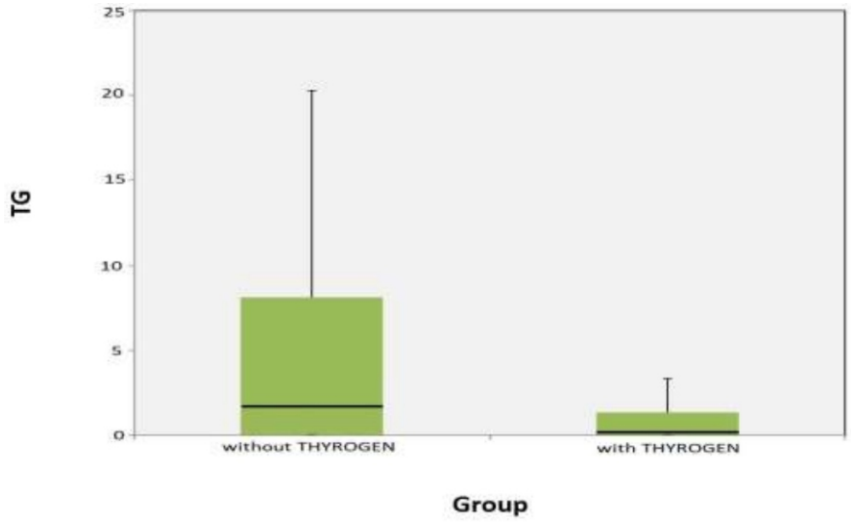


Figure 2: Comparing blood levels of Tg in the two groups using box plots. *Tg level is significantly higher in the patients who had stopped levothyroxine than the patients who receiving thyrotropin alfa.

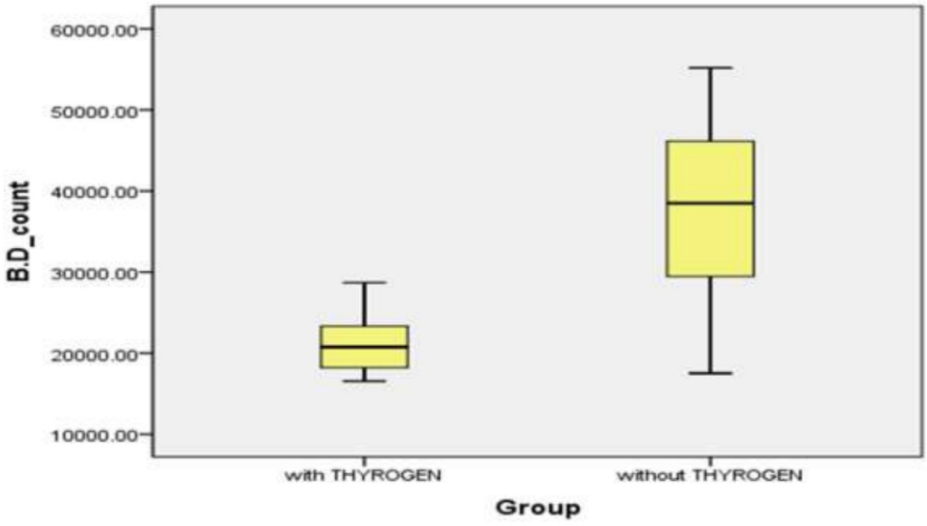


Figure 3: Comparing image quality with the body count parameter of the two studied groups using box plots. *Image quality is significantly higher in the patients who receiving thyrotropin alfa than the patients who had stopped levothyroxine.

DISCUSSION:

The present study results showed patients receiving thyrotropin alfa injections had a significantly higher TSH level than patients with THW. This rise in the TSH level after the thyrotropin alfa injection resulted in better image quality. In addition, the TSH level was kept high for a few days while using thyrotropin alfa injections; whereas, TSH was kept high for a few weeks when THW was used, which has proven to be associated with a lower probability of cancer reoccurrence accompanied by lower

levels of Tg. The patients with THW had a significantly higher TSH level than patients receiving thyrotropin alfa injections. The level of Tg must be very low after thyroidectomy. Therefore, if there was a detectable amount of Tg post-operation, it would be possible that a normal or cancerous thyroid tissue has remained in the patient's body or the tumor has recurred, indicating the need for additional treatment. As a result, the present study showed that the recurrence rate of the tumor was lower in patients receiving thyrotropin alfa injections than patients who had stopped consuming levothyroxine. Thyrotropin alfa is a protein produced by a recombinant DNA technique that is quite similar to TSH (18). Thyrotropin is consumed to measure thyroid activity, detect the amount of remnant thyroid after thyroidectomy, and increase the absorption of radioactive iodine by the thyroid gland (19, 20). Thyrotropin binds to thyrotropin receptors on residual thyroid cells or normal tissues, stimulating radioactive iodine uptake and improving diagnostic imaging quality with radioactive iodine (21). Measuring Tg levels can show if thyroid cancer cells are still in the body after treatment; that is, if Tg levels remain the same or increase after cancer treatment, it may indicate the presence of thyroid cancer cells in the body (22). If Tg levels decrease or disappear after treatment, it may mean that there are no normal or cancerous thyroid cells in the body. Follow-ups are performed after follicular or papillary cancer surgery by measuring Tg.

The lower the Tg, the lower the chance of recurrence, and vice versa (23-25). Tg levels are directly related to the tumor volume. Tg and TSH follow-ups are performed through annual periodic ultrasounds. The body count parameter is basically the count of ROI units in square meters, and if the amount increases in the imaging, it indicates that the image quality is low. As a result, the present study showed that due to the high body count in patients with THW, the image quality in patients receiving thyroid injections was higher than those with THW. Also, in this research, the quality of images was assessed based on the comments of nuclear medicine experts. The results showed that 65% of patients with thyrogen injection and 27.5% of patients with THW had good image quality. Therefore, there was a significant difference between the image quality of the two groups. During this period, several studies have been conducted in this regard with different results. Some of the said studies and their findings will be mentioned as follows, and their findings will be

compared with the present study results. In a study, Robbins et al. (2001) compared patient preparations by recombinant human thyrotropin (rhTSH) injection and discontinuation of the thyroid hormone to detect residual thyroid carcinoma in patients with thyroid cancer. In this retrospective study, 289 patients were studied for two years. These patients were divided into two groups.One group consisted of 161 patients with thyroid hormone withdrawal (THW). The second group consisted of 128 patients with thyroid hormone residue who received a thyrogen injection (rhTSH). The Diagnostic whole-body

radioiodine scanning (DxWBS) and Tg levels were measured for all patients after the rise of TSH. Sensitivity, specification, positive and negative predictive values of DxWBS and Tg stimulated after preparation were evaluated using THW and rhTSH methods. The results showed no significant difference between positive and negative predictive values of the two groups. The highest negative predictive value among patients (97%) was seen in patients with negative DxWBS, and low stimulated Tg levels after rhTSH. Overall, this study was unable to show significant differences in the diagnostic accuracy of DxWBS and/or Tg between patients prepared by THW or rhTSH. They concluded that the preparation of patients with rhTSH was diagnostically equivalent to preparation with THW (26). In contrast, the result of our study showed image quality of patients with thyrotropin alfa injections method was pereferd. In another study by Dontas et al. (2003), the use of thyrotropin alfa was examined in the treatment and diagnosis of thyroid cancer patients. They concluded that the introduction of rhTSH in the diagnosis of thyroid cancer improved the patient's quality of life by preventing debilitating hypothyroidism. They reported seven cases intending to update the use of thyrotropin alfa. All these seven cases were treated with thyrotropin alfa for diagnostic or therapeutic purposes. All seven patients underwent thyroidectomy, and the remnant thyroid cells were removed by radioactive iodine, and all had basal serum thyroglobulin levels (b-Tg) [1 ng/ml <]. Thyroid stimulation resulted in an increase in Tg (s-Tg) in all patients. Five patients had a negative whole body scan (WBS) and had no clinical or radiological symptoms. Two patients with Tg of 5 ng/ml and 11 ng/ml showed Tg of 17 ng/ml and 84 ng/ml, respectively, while their WBS was negative.

Both patients received 100 mCi I 131. Patients with positive values of Tg and WBS with cranial, lung, and liver metastases received I 131 after preparation with thyrotropin alfa. Six months later, one of these patients was disease-free, and the other was evaluated in the coming months. As a result, thyrotropin alfa appeared as a reliable factor in the diagnosis of thyroid cancer. In addition, it seemed that thyrogen could be used to metastasis as an alternative for THW. The result of this study indicated that the use of thyrotropin alfa was reliable and safe, and thyrotropin alfa was also a very good alternative for THW to treat metastatic thyroid cancer (27). Lipp (2014) conducted a study on the sensitivity of preparations with rhTSH and THW using an I131 WBS to detect thyroid cancer metastases. They based their study on a report that stated that rhTSH was more sensitive to the diagnosis of differentiated thyroid cancer (DTC) metastases than THW. The goal of their study was to confirm this reported difference in sensitivity using whole body scan (WBS). In this retrospective study, 43 patients with evidence or suspicion of metastatic DTC (assessed by Tg or abnormal findings in the previous WBS) underwent WBS 24 hours after oral consumption of 370 MBq I^{131}. Two independent observers interpreted WBS, and then categorized the findings as positive or negative for metastatic diseases. Findings were controlled by measuring stimulated Tg and a two-year follow-up.

Of the studied patients, preparations were done for 14 patients with rhTSH and 29 patients with THW. According to the results, there was no statistical difference between the characteristics of the patients in the two groups (age, sex, Tg level, TSH level, and type of cancer). In this study, no difference was observed between the WBS sensitivity of patients treated with rhTSH and patients with THW. Out of the studied 14 patients, 11 individuals (78%) were positive for rhTSH, and 19 out of 29 patients (65%) were positive for THW. Metastatic patients were confirmed by assessment and follow-up of stimulated Tg. The results of this study showed that, unlike previously published data, no difference was in the sensitivity of rhTSH or THW for the preparation of DTC patients under I^{131} imaging (28). Park et al. (2017) did a study on early stimulation of Tg after administration of thyrogen. It is generally recommended to measure the Tg stimulated by rhTSH 72 hours after the second rhTSH injection. However, due to the acute effect of I131 on thyrocytes, Tg is measured after radioiodine therapy (RIT) and is not accurately reflective of the load on thyroid tissue.

Their study aimed to determine the predictive value of serum Tg levels measured before RIT with the help of rhTSH and compare the post-RIT results in patients with disseminated thyroid carcinoma (DTC). In this study, patients with DTC after a complete thyroidectomy were studied between 2009 and 2014. The serum Tg level of these patients was measured 24 hours (primary Tg) and 72 (or 96) hours (Delayed or secondary Tg) after the rhTSH injection. An excellent response was defined according to the latest guidelines of the American Thyroid Association. Univariate and multivariate analyzes were performed for primary Tg, delayed Tg, and other clinical variables. In multivariate analysis, tumor size [odds ratio (OR) of 1.716; confidence interval (CI) of 95%; 1.019–2.882 p=0.042] and the primary Tg level (or 2.012; 95% CI; 1.384-2 0.925 CI, p<0.001) independently predicted excellent responses. The best primary Tg level was 2.0 Ng/ml for predicting an excellent response. The delayed Tg was not significantly predictive (OR=0.992; 95% CI 0.969-1 .015; p=0.492). Primary Tg stimulation after RIT significantly predicted therapeutic response in patients with DTC with the aid of rhTSH. Therefore, to predict therapeutic responses, serum Tg should be measured before RIT. Furthermore, it was concluded that injection of thyrotropin alfa had a significant effect on the amount of Tg reaching the therapeutic value (29).Klubo-Gwiezdzinska et al. (2013) studied the use of recombinant human thyrotropin in the treatment of distant metastases in patients with DTC. To effectively treat DTC with radioactive iodine (RAI), it is necessary to increase serum TSH levels through THW or by prescribing rhTSH. The objective of this study was to provide current data on the relative impact and specifications of the side effects of THW with the help of rhTSH and RAI for the treatment of patients with DTC metastases. They searched the PubMed database for articles containing the keywords "rhTSH," "thyroid cancer," and "distant metastases" published between Jan 1, 1996, and Jan 7, 2012.

They utilized a collection of clinical cases, reports, articles, and practical guidelines as resources. According to their findings, an increase in the TSH level with the injection of thyrotropin alfa was associated with a better quality of life because it eliminated the signs and symptoms of hypothyroidism caused by an increase in TSH through the THW method. The rate of neurological complications after RAI treatment with rhTSH and THW was similar for brain and spinal metastases. The rates of leukopenia, thrombocytopenia, pulmonary dryness, and fibrosis after preparation were also similar after preparation with rhTSH and THW for the RAI treatment. Currently, there is a discrepancy in some studies on the RAI uptake in metastatic lesions after preparation with rhTSH versus THW. Some studies argue that the uptake is equal for both methods and others emphasize the superiority of THW. Analyzing the existing retrospective studies comparing survival, progression-free survival, and biochemical and structural responses to set RAI dosimetry reported similar effects after preparation through rhTSH and THW. Stimulation of rhTSH is currently approved by the FDA as preparation for adjuvant therapy with RAI in patients with metastatic DTC. Data on rhTSH stimulation show that rhTSH stimulation is as effective as THW as preparation for dosimetry-based RAI in treating distant metastases in patients with DTC (30).

CONCLUSION

The TSH biomarker was higher in patients receiving thyrotropin alfa injections, which properly prepared them for a thyroid nuclear scan without the patients' developing symptoms of hypothyroidism. The Tg level was higher in patients who had discontinued levothyroxine, indicating the probability of recurrence of the disease, metastasis, and/or residual thyroid tissue. The body count parameter was higher in patients with THW, which showed that the image quality was lower in this group than the group receiving thyrotropin alfa injections. Besides, the image quality was better in the thyrotropin alfa injections group. Therefore, based on the research results, receivingThyrogen injections was preferable to discontinuation of levothyroxine.

REFERENCES

1. Ho AS, Davies L, Nixon IJ, Palmer FL, Wang LY, Patel SG, et al. Increasing diagnosis of subclinical thyroid cancers leads to spurious improvements in survival rates. Cancer. 2015;121(11):1793-9.

2. Olson E, Wintheiser G, Wolfe KM, Droessler J, Silberstein PT. Epidemiology of thyroid cancer: a review of the National Cancer Database, 2000-2013. Cureus. 2019;11(2).

3. Pool EH, Falk HC. Concerning the surgical anatomy of the thyroid with special reference to the parathyroid glands. Annals of surgery. 1916;63(1):71.

4. Koubassov R, Yu B, Yu Y. Hypophysis-thyroid regulation features at different professional law-enforcement officer groups. International Journal of Collaborative Research on Internal Medicine &

Public Health. 2012;4(5):0-.

5. Hansen PS, Brix TH, Sørensen TI, Kyvik KO, Hegedüs L. Major genetic influence on the regulation of the pituitary-thyroid axis: a study of healthy Danish twins. The Journal of Clinical Endocrinology & Metabolism. 2004;89(3):1181-7.

6. Schroeder AC, Privalsky ML. Thyroid hormones, t3 and t4, in the brain. Frontiers in endocrinology. 2014;5:40.

7. Hertz S, Roberts A, Evans RD. Radioactive iodine as an indicator in the study of thyroid physiology. Proceedings of the Society for Experimental Biology and Medicine. 1938;38(4):510-3.

8. Schlumberger M, Mancusi F, Baudin E, Pacini F. 131I therapy for elevated thyroglobulin levels. Thyroid. 1997;7(2):273-6.

9. Spencer CA, Wang C-C. Thyroglobulin measurement: techniques, clinical benefits, and pitfalls. Endocrinology and metabolism clinics of North America. 1995;24(4):841-63.

10. Lin K-J, Huang J-Y, Chen Y-S. Fully automatic region of interest selection in glomerular filtration rate estimation from 99m Tc-DTPA renogram. Journal of digital imaging. 2011;24(6):1010-23.

11. Koundal D, Gupta S, Singh S. Computer aided thyroid nodule detection system using medical ultrasound images. Biomedical Signal Processing and Control. 2018;40:117-30.

12. Sager S, Hatipoglu E, Gunes B, Asa S, Uslu L, Sönmezoğlu K. Comparison of day 3 and day 5 thyroglobulin results after thyrogen injection in differentiated thyroid cancer patients. Therapeutic advances in endocrinology and metabolism. 2018;9(6):177-83.

13. Mat Nawi N, Ahmad NS, Abdullah R, Wan Zainon WMN, Abdul Razab MKA. Correlation of external dose rate with whole body clearance estimation in radioiodine therapy for rhTSH and THW patients. Journal of Radiation Research and Applied Sciences. 2020;13(1):240-5.

14. Lee J, Yun MJ, Nam KH, Chung WY, Soh E-Y, Park CS. Quality of life and effectiveness comparisons of thyroxine withdrawal, triiodothyronine withdrawal, and recombinant thyroid-stimulating hormone administration for low-dose radioiodine remnant ablation of differentiated thyroid carcinoma. Thyroid. 2010;20(2):173-9.

15. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, et al. 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the American Thyroid Association guidelines task force on thyroid nodules and differentiated thyroid cancer. Thyroid. 2016;26(1):1-133.

16. MAZZAFERRI EL. An overview of the management of papillary and follicular thyroid carcinoma. Thyroid. 1999;9(5):421-7.

17. Weitzel JM, Iwen KAH, Seitz HJ. Regulation of mitochondrial biogenesis by thyroid hormone. Experimental physiology. 2003;88(1):121-8.

18. Verburg FA, Aktolun C, Chiti A, Frangos S, Giovanella L, Hoffmann M, et al. Why the European

Association of Nuclear Medicine has declined to endorse the 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer. Springer; 2016.

19. Rosário PW, Borges MAR, Purisch S. Preparation with recombinant human thyroid-stimulating hormone for thyroid remnant ablation with 131I is associated with lowered radiotoxicity. Journal of Nuclear Medicine. 2008;49(11):1776-82.

20. Rizvi T, Rehm PK. Recombinant human thyrotropin use resulting in ovarian hyperstimulation: an unusual side effect. European thyroid journal. 2014;3(2):125-9.

21. Simon JE. Thyrogen® Scans for Detecting Recurrent Thyroid Cancer. Journal of Radiology Nursing. 2012;31(4):144-8.

22. Schuster H. Finding the Homeostatic Set Point of the Hypothalamus-Pituitary-Thyroid Axis with Different Modelling Approaches: Wien; 2021.

23. Stathatos N. Thyroid Physiology. Medical Clinics of North America. 2012;96(2):165-73.

24. Vanderpump MP. The epidemiology of thyroid disease. British medical bulletin. 2011;99(1).

25. BURMAN KD. Is long-term levothyroxine therapy safe? Archives of internal medicine. 1990;150(10):2010-3.

26. Robbins RJ, Tuttle RM, Sharaf RN, Larson SM, Robbins HK, Ghossein RA, et al. Preparation by recombinant human thyrotropin or thyroid hormone withdrawal are comparable for the detection of residual differentiated thyroid carcinoma. The Journal of Clinical Endocrinology & Metabolism. 2001;86(2):619-25.

27. Duntas LH, Tsakalakos N, Grab-Duntas B, Kalarritou M, Papadodima E. The use of recombinant human thyrotropin (Thyrogen) in the diagnosis and treatment of thyroid cancer. HORMONES-ATHENS-. 2003;2:169-74.

28. Liepe K. Sensitivity of preparation with rhTSH or thyroid hormone withdrawal using 131I-whole body scans to identify metastases of differentiated thyroid cancer. International Journal of Surgery. 2015;16:107-12.

29. Park HJ, Min J-J, Bom H-S, Kim J, Song H-C, Kwon SY. Early stimulated thyroglobulin for response prediction after recombinant human thyrotropin-aided radioiodine therapy. Annals of nuclear medicine. 2017;31(8):616-22.

30. Klubo-Gwiezdzinska J, Burman KD, Van Nostrand D, Mete M, Jacqueline J, Wartofsky L. Potential use of recombinant human thyrotropin in the treatment of distant metastases in patients with differentiated thyroid cancer. Endocrine Practice. 2013;19(1):139-48.

ISSN: Print -0976-9234

To Investigate The Prevalence And Incidence Of Anaemia And Its Comorbidities In The Gandhinagar Population

Heenaben A. Chokshi1*, Vaibhav Arvindbhai Joshi2, Dr. Gaurang B Shah3 , Dr. Maulikkumar D. Vaja4, Ms. Payal M. Vaghela5, Sneha P. Dave6

1*Heenaben A. Chokshi, Department of Pharmacology and Pharmacy Practice, Saraswati Institute of Pharmaceutical Sciences, Dhanap, Gandhinagar -382355, Gujarat, India. ORCID: 0000-0003-1125-9408, Email Id: hacsips@yahoo.com, 2Manager- Business development, COD Research Private Limited, 301, I Square Near Shukan Mall, Science City Rd, Sola, Ahmedabad, Gujarat 380060 Email id: vaibhav.joshi175@gmail.com, 3Professor – Department of Pharmacology, L. M. College of Pharmacy, MG Science College Rd, opp. gujarat university, University Area, Ahmedabad, Gujarat 380009, Email id: gaurang.shah@lmcp.ac.in, 4Associate Professor, Department of pharmaceutical chemistry Saraswati Institute of Pharmaceutical Sciences, Dhanap, Gandhinagar - 382355, Gujarat, India, Email id: maulikvajaniper@gmail.com, 5Assistant Professor, C. U. Shah Institute of Nursing, C. U. Shah University, Wadhwan, Surendranagar, Gujarat-363030 India. Email id: vaghelapayal449@gmail.com, 6Associate Professor, Saraswati Institute of Pharmaceutical Sciences, Department of Pharmacognosy Dhanap, Gandhinagar - 382355, Gujarat, India.

A B S T R A C T

Background: Anaemia is a major public health issue that affects 2 billion people worldwide, affecting people of all ages and genders. According to the WHO, iron deficiency anaemia is the leading cause of anaemia, accounting for 50% of all cases.Methodology: An observational study was carried out at Gandhinagar, Gujarat from November 2015 to March 2016. A complete blood count (CBC) report of patients were collected directly from patient's laboratory report and entered in structured case report form. The Questionnaire, to obtain information regarding life style, food habits, socioeconomic status and medical history was filled by the patients. Results: A total of 521 patient's data were collected in which 146 (48.66%) males and 154 (51.33%) females were suffering from anaemia. In anaemic patients 131 (43.66%) patient were microcytic anaemic, 125 (41.66%) were normocytic and 44 (14.66%) patientwere macrocytic anaemic. Out of 300 anaemic patients, 231 (76.15%) were in age group of 16-50 years. Majority of patients seems to be suffering from the nutritional anaemia due to poor consumption of diet. Majority of anaemic patients belonged to upper-middle class and upper-lower class family. There were no significant differences of the smoking, tobacco, alcohol consumption with anaemia.Conclusion: According to our data, poor dietary habits seem to be major cause for anaemia. Lack of awareness about the disease worsens the problem. Awareness programs at community levels by health agencies can significantly help in reducing the burden of the diseases.

Keywords: Anaemia causes, IDA, Iron deficiency anaemia, global public health, ACD

INTRODUCTION

Anaemia is a medical condition in which the red blood cell (RBC) count or haemoglobin level is lower than normal.[1,2]Anaemia is mostly brought on by viral diseases including malaria, hookworm infections, and schistosomiasis, shortages of other important micronutrients like folate, vitamin B12, and vitamin A, or inherited disorders that damage red blood cells (RBCs), such thalassemia.[3-6]Iron is very essential for the formation of Red blood cells, anaemia can develop from a decrease in red blood cell formation caused by a lack of iron in the body.[7-9]It is a common condition,affecting an estimated 3.5 billion people worldwide, including both children and adults. Anaemia, whichaffects 2 billion people globally and affects both sexes and all age groups, is a serious public health issue.[10-12] According to the WHO, iron deficiency anaemia was the main cause of anaemia in 50% of cases.[13-15], but other factors can contribute to the development of the disease, such as chronic inflammation, blood loss due to menstruation or ulcers, and certain diseases or conditions.[16-18]In these circumstances, anaemia sets in because the body is unable to replenish lost red blood cells in a timely manner. As a result, anaemia was seen to be more common in developing countries (43%), compared to developed countries (9%).[19-21] Anaemia can have serious implications for health, including fatigue, impaired cognitive function, and a weakened immune system.[13,22,23] The goal of the current study was to determine the prevalence of anaemia and its related complications in the residents of the Gandhinagar, Gujarat region by implementing observational research between November 2015 and March 2016. The data was collected in a structured case report format, a complete blood count (CBC) report for each patient was obtained directly from the patient's laboratory report and the patients filled out a questionnaire to provide details on their lifestyle, eating habits, socioeconomic background, and medical information.

MATERIALS AND METHODOLOGY

The entire study is based on secondary analysis that relies on works of literature and research materials provided by eminent scholars and professional medical practitioners. The reference to the relevant articles and medical reports relaying results from research conducted by the professional on a variety of cases of Anaemia and different demographic and conditional associations, followed by cases of exception, has helped in developing the discussion in the study. Hence, for the purpose of the study previous reports and articles are the main materials that would help in accomplishing the study, and the applied methodology encircles the case study-specific secondary research approach. A study protocol was created and submitted to the Gandhinagar-based K.B. Institute of Pharmaceutical Education and Research's institutional ethics committee. Project approval has been given (Protocol number: KBIEC/2015/59).

Inclusion criteria

• Patients undergoing full blood counts were involved in the trial,

• Patients' willingness to take part in the study and sign informed permission forms was also a requirement.

Exclusion criteria

• People who suffer from chronic renal failure

• Patients taking cytotoxic or anticancer medications

• People who have sickle cell anaemia, thalassemia, or other chronic haematological diseases that run in their families.

• Individuals who have recently been introduced to radioactive materials.

Based on a literature review, a self-generated questionnaire was created that asks about socio-demographic factors like age, educational attainment, family structure, monthly income, dietary history, and pertinent medical histories like hypertension, malaria, and worm infestation. In order to gather information about the patients' education, employment status, and family income, a modified Kuppuswami scale was used. A questionnaire was utilised to gather data from the patient regarding their socioeconomic status, sociodemographic characteristics, dietary habits, and medical history. The results were expressed in terms of number and percentage. The data were analysed by using the Spearman rank coefficient to determine a correlation between different risk factors and the severity of anaemia.

Sample size:

300–500 anaemic patients were enrolled in accordance with the inclusion criteria.

Study procedure:

The patients were selected on the basis of inclusion and exclusion criteria.

The patients filled the informed consent form prior to inclusion in the study.

The questionnaire was used to collect the information from patient about socioeconomic, socio-demographic, food intake and medical history.

The data analysis was done by using Spearman rank correlation and one way ANOVA test.

Statistical analysis:

The results were expressed in terms of number and percentage. The data were analysed by using the Spearman rank coefficient to determine the correlation between different risk factors and the severity of anaemia. One-way ANOVA followed by post-hoc Tukey's test using graph pad prism wasconducted to determine statistical significance between the two groups. P value of less than 0.05 was considered a significant difference.

RESULTS

The complete blood count reported of subjects approaching the pathology lab was recorded. Additionally, a questionnaire on signs & symptoms and their lifestyle was provided to them. The data obtained through them were analysed and the obtained results are summarized here.

1. Prevalence of anaemia in subjects undergoing haematocrit analysis:

Three hundred of five hundred twenty one subjects were found to have haemoglobin levels less than 12 g and were closed as anaemic. One of this 300 anaemic subjects 208(69.33%) had mild anaemia (hb: 10-12g), 72(24g) had moderate (hb: 10-7g) and 20(6.66g) had severe anaemia (hb: <7g) (Figure 1).

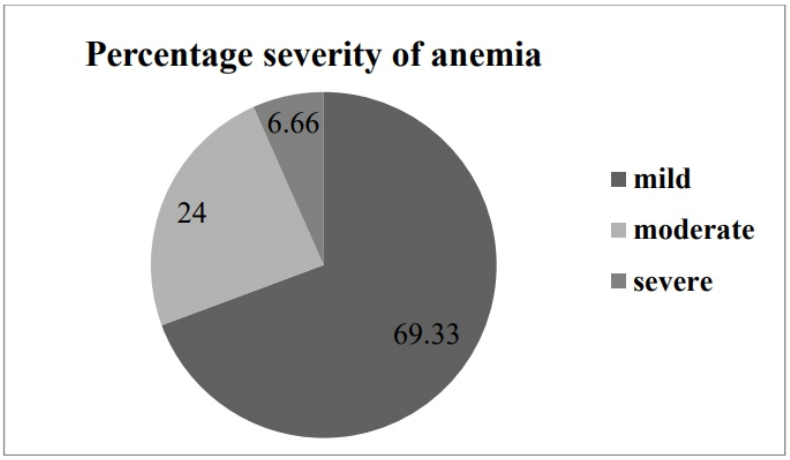


Figure 1 Percentage severity of anaemia

2. Types of anaemia based on RBC size:

Based on Mean Corpuscular Volume (MCV) value, the anaemic subjects were further categorized as

microcytic, normocytic and macrocytic anaemic subjects. Microcytic anaemia in 131 subjects (43.66%), Normocytic anaemia was found in 125 subjects (41.66%) and Macrocytic anaemia was found in 44 subjects (14.66%) (Figure 2).

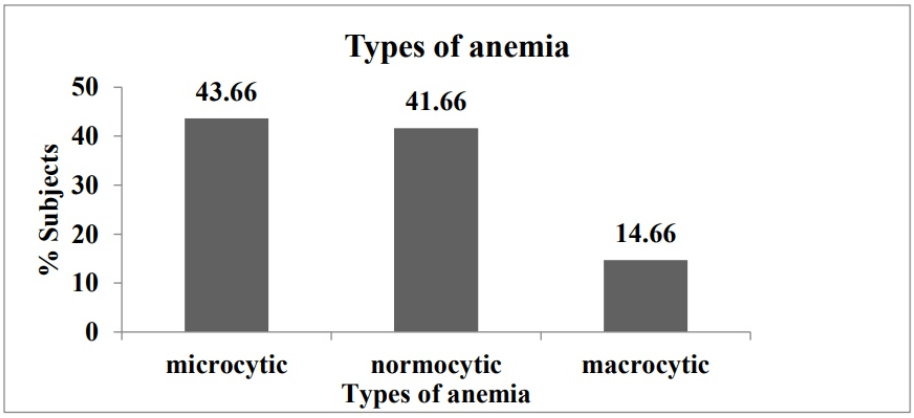


Figure 2: Types of anaemia

Demographic details of subjects:

Age wise distribution of anaemic subjects:

Most subjects who had anaemia fall in to the age group of 40-49 years (30%). Only 5% fall into 16-19 years age group and 8% fall in the age above 60 years group. The age wise prevalence of anaemia is summarized in the (Figure 3).

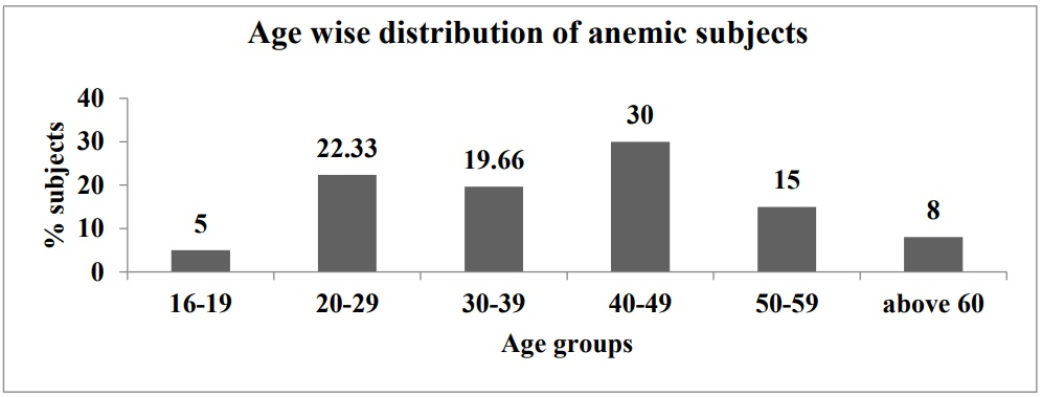


Figure 3 The figure represents distribution of anaemic subjects in various age groups. Each bar represents percentage of anaemic subjects in particular age groups.

Residence status of anaemic subjects:

The numbers of anaemic patients enrolled in the study according to their residence were categorized in to urban and rural in which 77.33% patients belonged to urban area whereas 22.66% patients belonged to rural area (Figure 4).

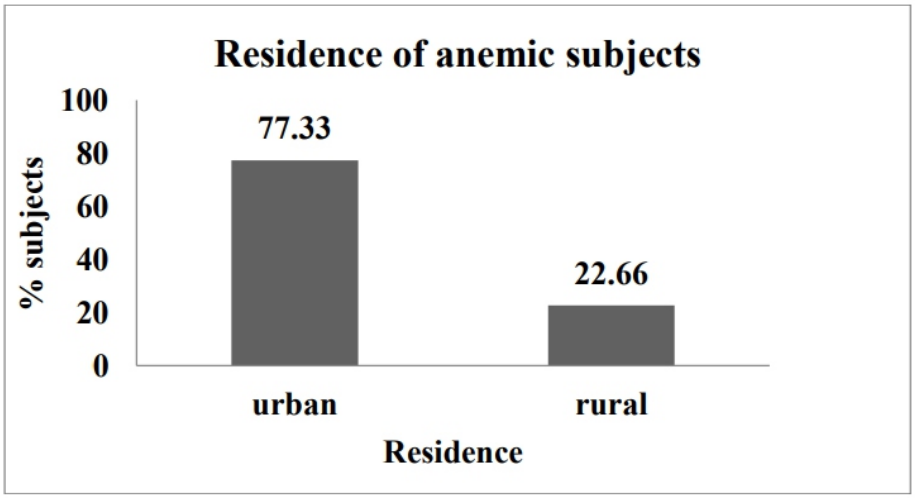


Figure 4 Residence status of anaemic subjects

Socioeconomic status:

Each bar in the (Figure 5) indicates the socioeconomic status of the subjects. The maximum number of subjects enrolled in the study was from the upper middle class 39.66% the patients who belonged to the upper class were 12%, the lower middle class were 19.33% and the upper lower class was 29% respectively. The lower class could not report their status due to their financial inability.

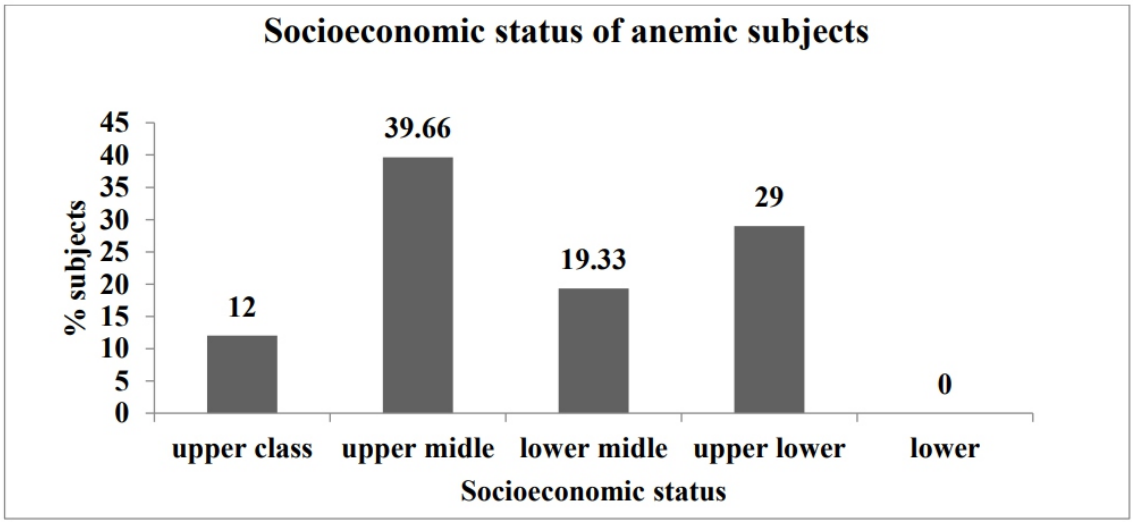


Figure 5 Socioeconomic status

3. Addiction: Smoking habits:

The figure indicates the smoking habits of the subjects. The subjects with the anaemic conditions had smoking habits of 18.42% and non-anaemic subjects had 19.81% (Figure 6).

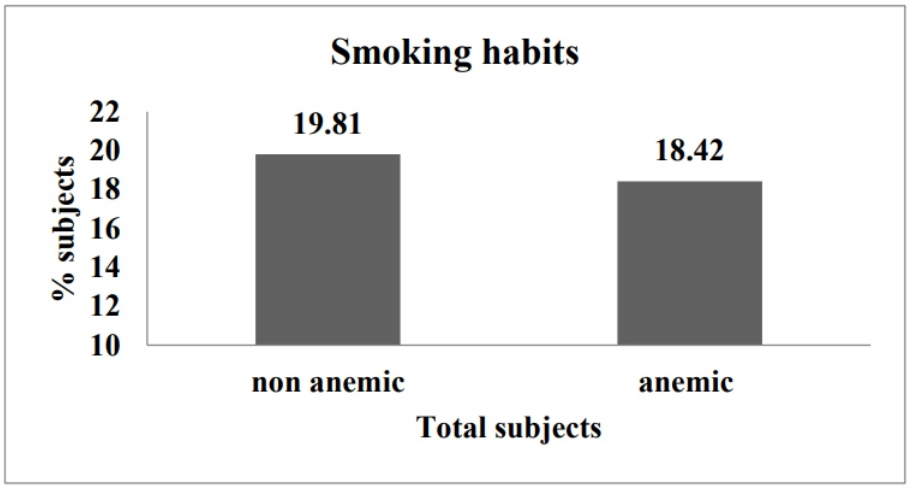


Figure 6 Smoking Habits

Tobacco habits:

The figure indicates the Tobacco habits of the subjects. The subjects with the anaemic conditions had tobacco habits of 7.89% and non-anaemic subjects had 5.52% (Figure 7).

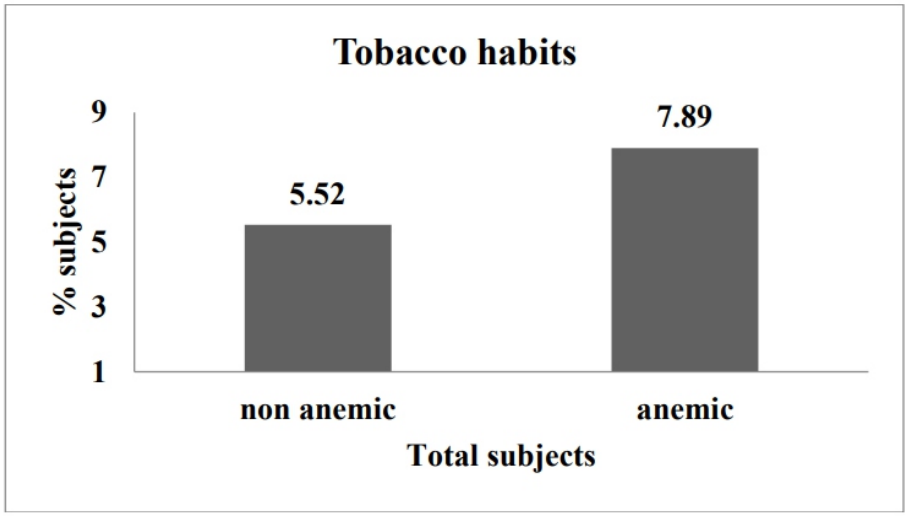


Figure 7 Tobacco Habits

Alcohol consumption:

The figure indicates the alcohol consumption of the subjects. The subjects with the anaemic conditions had alcohol consumption habits of 9.21% and non-anaemic subjects had 8.75% (Figure 8).

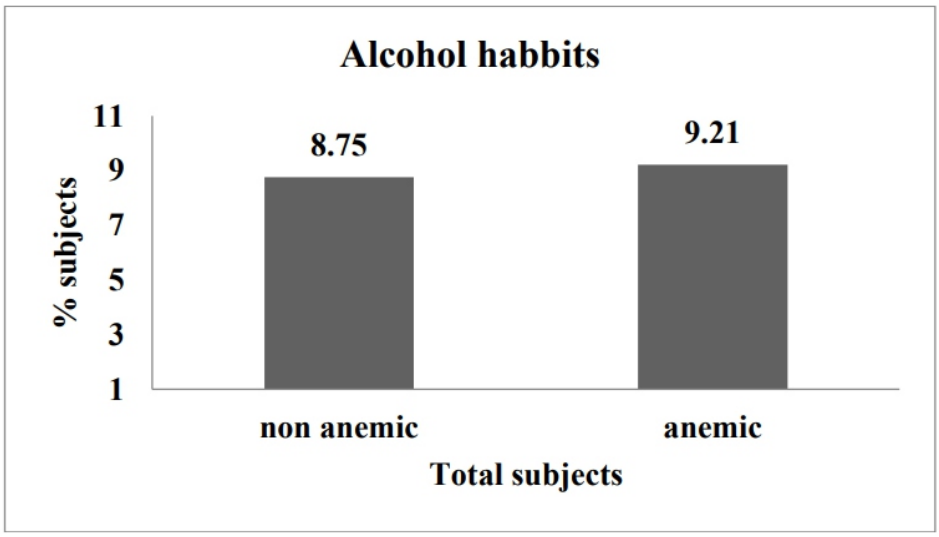


Figure 8 Alcohol Habits

Tea habits:

The figure indicates the tea consumption habits of the subjects. The subjects with the anaemic conditions had tea consumption habits of 86.84% and non-anaemic subjects had 84.79% (Figure 9).

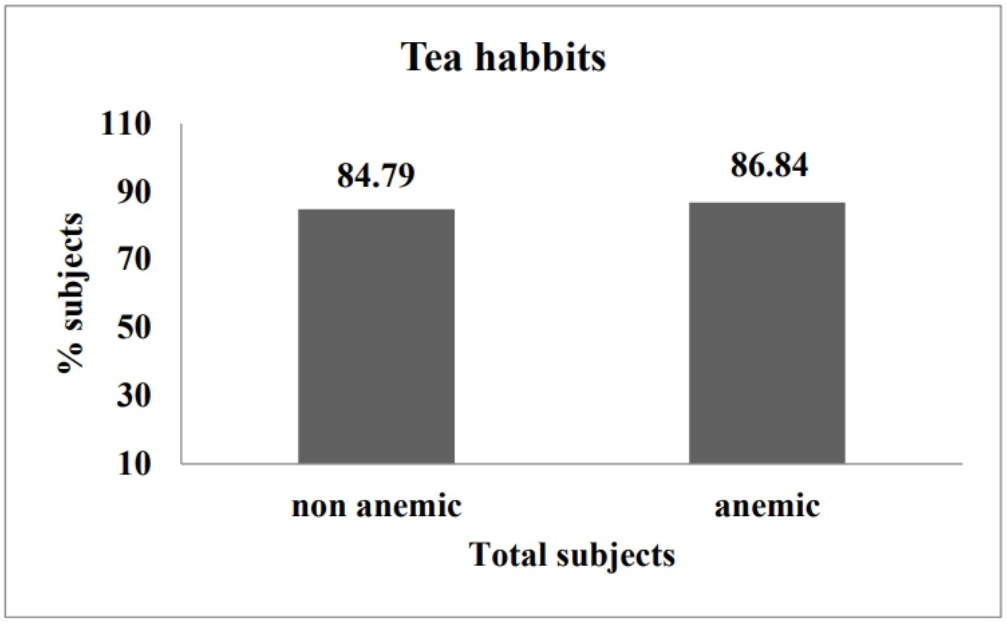


Figure 9 Tea Habits

Diet:

Comparison of the frequency of consumption of macronutrient rich diet in anaemic and non-anaemic subjects is given below:

Protein: The frequency of consumption of protein was found to be higher in normocytic anaemic subjects than in the microcytic and macrocytic subjects. In addition to that the protein in consumption

was observed significantly higher in non-anaemic subjects. (*= <0.05, **= <0.01, ***= <0.001, ****= <0.0001) (Figure 10).

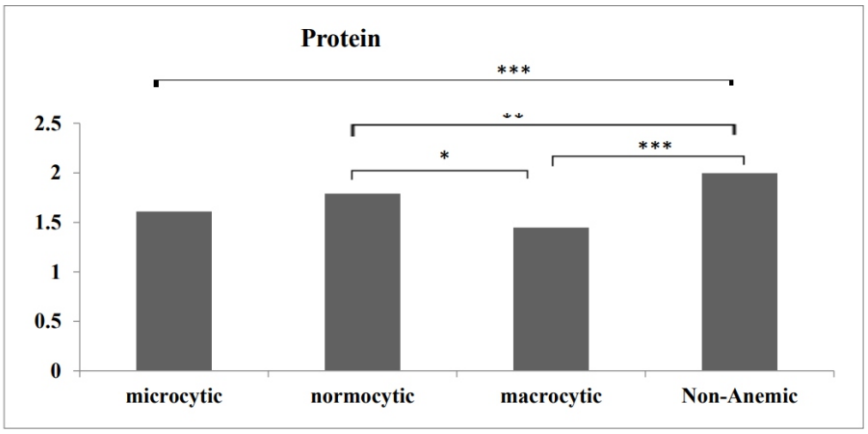


Figure 10 Consumption of Protein

Carbohydrate:

The frequency of consumption of carbohydrates was found to be higher in non-anaemic subjects than the microcytic and macrocytic subjects. In addition to that carbohydrate in consumption was observed significantly in microcytic and non anaemic subjects. (*= <0.05, **= <0.01, ***= <0.001, ****= <0.0001) (Figure 11)

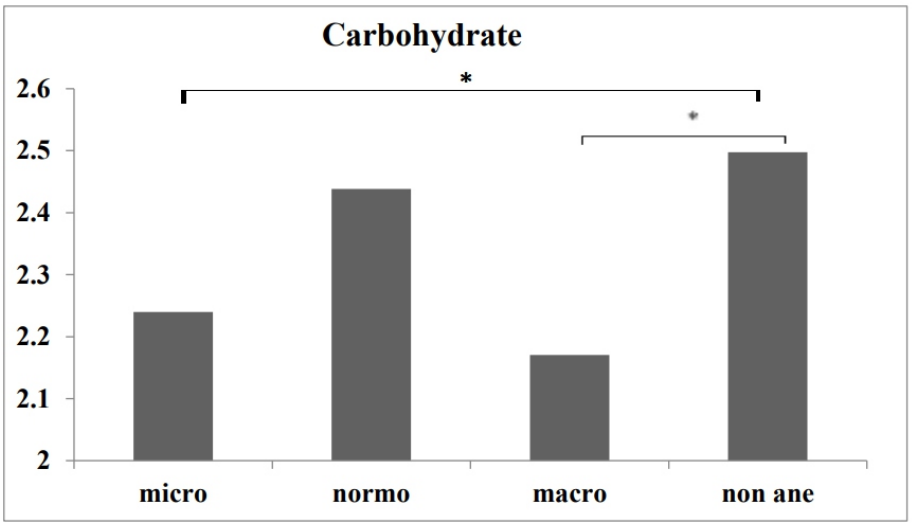


Figure 11 Consumption of carbohydrates

Fat:

There was a significant difference in macrocytic and non-anaemic subjects. (*= <0.05, **= <0.01, ***= <0.001, ****= <0.0001) (Figure 12).

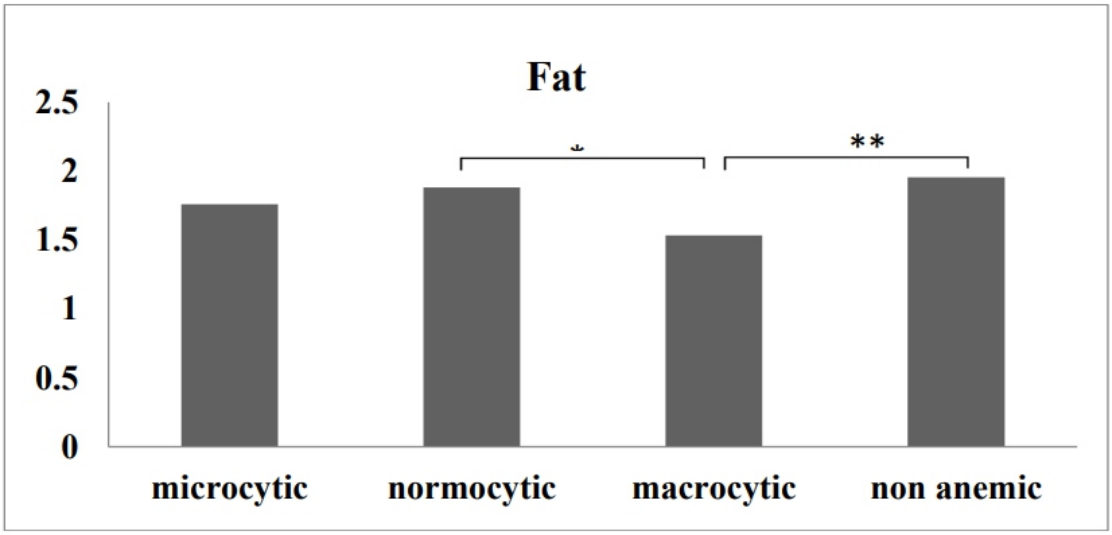


Figure 12 Consumption of fat

6. Comparison of frequency of consumption of macronutrient rich diet in anaemic and non-anaemic subjects: Vitamins:

The consumption of vitamins in subjects shows a significant difference in microcytic anaemia and non-anaemic subjects. (*= <0.05, **= <0.01, ***= <0.001, ****= <0.0001) (Figure 13).

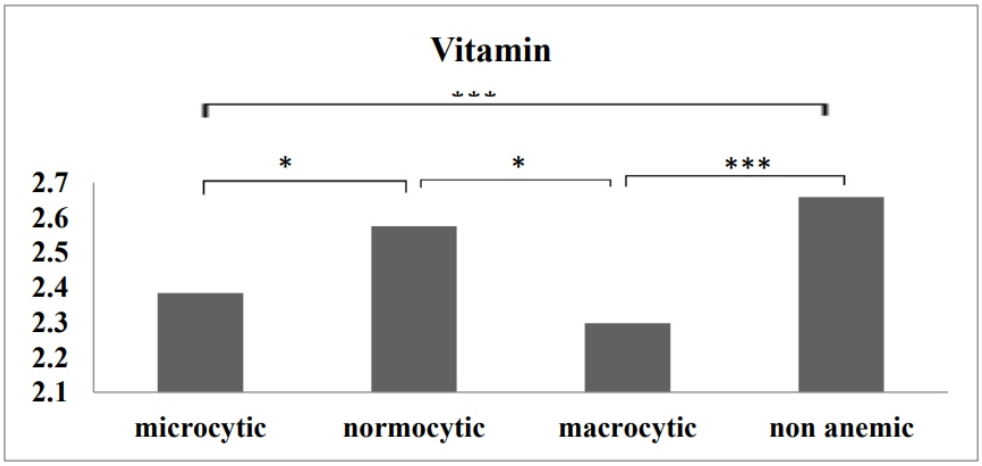


Figure 13 Consumption of vitamins

Minerals:

The frequency of consumption of minerals in subjects was a significant difference in normocytic anaemia and nonanaemic subjects. (*= <0.05, **= <0.01, ***= <0.001, ****= <0.0001) (Figure 14).

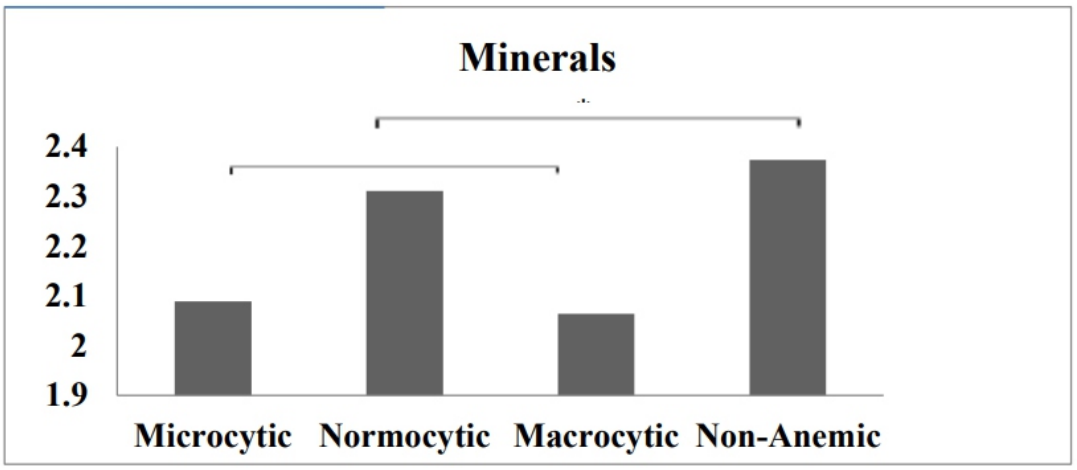


Figure 14 Consumption of minerals

7. The distribution of subjects according to their co-morbidity:

The percentage indicates the co-morbidity found in anaemic subjects, in which it was found that the majority of subjects were suffering from chronic hypertension and considerable (10.33%) subjects were suffering from diabetes mellitus. It was observed that 48% of subjects were having no co-morbidities (Table 1) (Figure 15).

Table 1 Co-morbidity

No.	Co-morbid	Percentage (%)
1	Chronic hypertension	**17.33**
2	Diabetes Mellitus	**10.33**
3	Renal diseases	6.00
4	Rheumatoid arthritis	5.33
5	Hypothyroid	4.06
6	Malaria	3.66
7	Jaundice	3.00
8	T.B	2.00
9	General warm infection	1.66
10	Depression	0.66
11	cardiac diseases	0.66
12	History of bleeding other than menstruation and delivery	0.66
13	Amebiasis infection	0.33
14	None	48

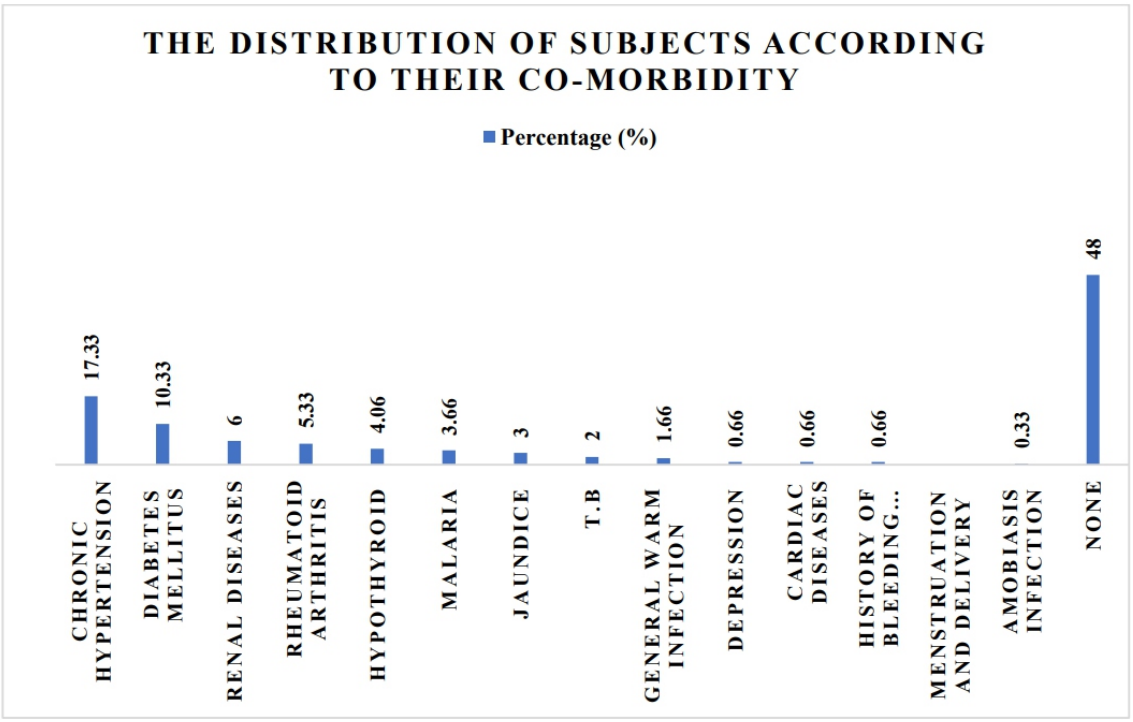


Figure 15 Co-morbidity

8. Symptoms of anaemia: Percentage severity of symptoms of anaemia are given below (Table 2) (Figure 16):

Table 2 Percentage (%) severity of symptoms in anaemia

Symptoms	Non-anaemia (n=221)	Mild anaemia	Moderate anaemia	Severe anaemia
Chest pain	6.91	10.62	20.27	13.04
Shortness of breath	7.83	8.21	18.91	30.43
Palpitation	15.20	18.84	35.13	26.08
Irritability	23.04	27.53	44.59	34.78
Decrease exercise tolerances	6.91	10.62	25.67	17.39
Fatigue	20.27	29.46	54.05	47.82
Dizziness	15.20	47.82	39.18	21.73
Weakness	51.15	69.56	74.32	65.21
Vertigo	10.13	12.07	36.48	26.08

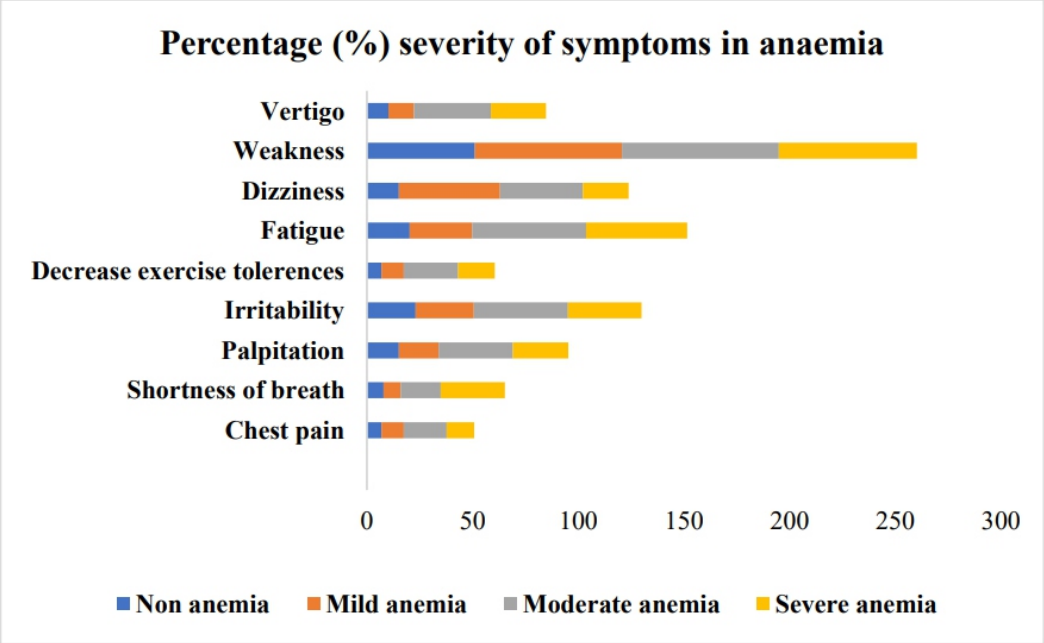


Figure 16 Percentage (%) severity of symptoms in anaemia

DISCUSSION:

Anaemia is a common and potentially serious disorder that can have a significant impact on the health and well-being of an individual [24,25]and can also have a significant influence on an individual's quality of life.[26]It has been linked to a wide variety of symptoms, some of which include fatigue, weakness, and impaired cognitive functioning.[27-30] While there are numerous causes of anaemia, the most common is iron deficiency. Iron deficiency anaemia can be treated through dietary interventions, supplementation and in severe cases, blood transfusions.[27,31-33] While anaemia can be diagnosed, it is a treatable condition with an excellent prognosis.[34-36]It is therefore important for healthcare practitioners to be aware of the signs, symptoms and treatments associated with anaemia, so that early diagnosis and management can be achieved.[37-39] Through proper diagnosis and treatment, individuals can return to their previous levels of health and functioning. It is important to recognize the signs and symptoms of anaemia in order to identify those at risk and ensure they receive the appropriate medical care. With proper diagnosis and management, anaemia can be managed and individuals can lead healthy lives free from its debilitating effects. [39-42]It is important to remember that anemia is multifactorial, and its occurrence may be due to the presence of cancer, inflammatory diseases, kidney disease, diabetes, hypertension, and the use of several drugs commonly required in the elderly population.[43-47] Nevertheless, further investigations of the cause of anemia and the completion of treatment may help to improve clinical conditions in the elderly population.

CONCLUSION AND FUTURE PROSPEC- TIVE:

In our study, we included a total of 521 patient records, and anaemia was present in 146 (48.66%) of the male patients and 154 (51.33%) of the female patients. In anaemic individuals, 44 (14.66%) had macrocytic anaemia, 131 (43.66%) had microcytic anaemia, and 125 (41.66%) had normocytic anaemia. Total number of 231 (76.15%) of the 300 anaemic patients were between the ages of 16 and 50. The majority of individuals appear to have nutritional anaemia as a result of poor diet consumption and also vitamins, minerals, and proteins all significantly correlated with most anaemic patients came from upper-middle class or upper-lower class families. The relationship between anaemia and smoking, drinking, or using tobacco was not significantly different.In the future, further research needs to be conducted on anaemia in order to better understand its causes, symptoms and possible treatments. Additionally, research should look into how to better educate individuals on anaemia prevention and management strategies.[48-50] The future prospect should also focus on the development of novel treatments for anaemia. As the understanding of anaemia increases, so too will our ability to develop effective treatments and improve the quality of life for those living with the condition.

CONFLICT OF INTEREST:

The authors declare no conflict of interest regarding this work.

FUNDING:

None

REFERENCES:

1. Vieth JT, Lane DR. Anemia. Emergency Medicine Clinics. 2014;32(3):613-628.

2. Chaparro CM, Suchdev PS. Anemia epidemiology, pathophysiology, and etiology in low-and middle-income countries. Annals of the new York Academy of Sciences. 2019;1450(1):15-31.

3. Rammohan A, Awofeso N, Robitaille M-C. Addressing female iron-deficiency anaemia in india: is vegetarianism the major obstacle? International Scholarly Research Notices. 2012;2012

4. Shulman C, Graham WJ, Jilo H, et al. Malaria is an important cause of anaemia in primigravidae: evidence from a district hospital in coastal Kenya. Transactions of the Royal Society of Tropical Medicine and Hygiene. 1996;90(5):535-539.

5. Bhadra P, Deb A. A review on nutritional anemia. Indian Journal of Natural Sciences. 2020;10(59):18466-18474.

6. Al Khatib L, Obeid O, Sibai A-M, Batal M, Adra N, Hwalla N. Folate deficiency is associated with

nutritional anaemia in Lebanese women of childbearing age. Public health nutrition. 2006;9(7):921-927.

7. Pattnaik S, Patnaik L, Kumar A, Sahu T. Prevalence of anemia among adolescent girls in a rural area of Odisha and its epidemiological correlates. Indian Journal of Maternal and Child Health. 2013;15(1):5.

8. Johnson-Wimbley TD, Graham DY. Diagnosis and management of iron deficiency anemia in the 21st century. Therapeutic advances in Gastroenterology. 2011;4(3):177-184.

9. Adamson JW. Regulation of red blood cell production. The American journal of medicine. 1996;101(2):4S-6S. 10. Ratre B, Patel N, Patel U, Jain R, Sharma V. Clinical and epidemiological profile of anemia in central India. Int J Med Res Rev. 2014;2(1):45-52.

11. Chellamani A. A Study to evaluate the Effectiveness of nutrition ball on haemoglobin level among adolescent girls with iron deficiency anaemia at selected industry Hostel in Madurai. College of Nursing, Madurai Medical College, Madurai; 2014.

12. Gupta A. Nutritional anemia in preschool children. Springer; 2017.

13. Deshpande NS, Karva D, Agarkhedkar S, Deshpande S. Prevalence of anemia in adolescent girls and its co-relation with demographic factors. International Journal of Medicine and Public Health. 2013;3(4)

14. Stoltzfus RJ. Defining iron-deficiency anemia in public health terms: a time for reflection. The Journal of nutrition. 2001;131(2):565S-567S.

15. Miller JL. Iron deficiency anemia: a common and curable disease. Cold Spring Harbor perspectives in medicine. 2013;3(7):a011866.

16. Qureshi NA, Chauhan MAZ, Goswami A, Suri S. Study of anemia and its correlation with Hematological parameters in patient of various age group. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS). 2015;14(9):29-35.

17. Weiss G, Ganz T, Goodnough LT. Anemia of inflammation. Blood, The Journal of the American Society of Hematology. 2019;133(1):40-50.

18. Jaul E, Barron J, Rosenzweig JP, Menczel J. An overview of co-morbidities and the development of pressure ulcers among older adults. BMC geriatrics. 2018;18(1):1-11.

19. Verma A, Rawal V, Kedia G, Kumar D, Chauhan J. Factors influencing anaemia among girls of school going age (6-18 years) from the slums of Ahmedabad city. Indian Journal of Community Medicine. 2004;29(1):25.

20. Scrimshaw NS. Iron deficiency. Scientific American. 1991;265(4):46-53.

21. Yip R, Ramakrishnan U. Experiences and challenges in developing countries. The Journal of nutrition. 2002;132(4):827S-830S.

22. Bentley ME, Griffiths PL. The burden of anemia among women in India. European journal of

clinical nutrition. 2003;57(1):52-60.

23. Mack P, Freedman J. Autoimmune hemolytic anemia: a history. Transfusion medicine reviews. 2000;14(3):223-233.

24. Patterson AJ, Brown WJ, Powers JR, Roberts DC. Iron deficiency, general health and fatigue: results from the Australian Longitudinal Study on Women's Health. Quality of Life Research. 2000;9:491-497.

25. Mirza FG, Abdul-Kadir R, Breymann C, Fraser IS, Taher A. Impact and management of iron deficiency and iron deficiency anemia in women's health. Expert review of hematology. 2018;11(9):727-736.

26. Sobrero A, Puglisi F, Guglielmi A, et al. Fatigue: a main component of anemia symptomatology. Elsevier; 2001:15-18.

27. Bansal B, Takkar J, Soni N, Agrawal DK, Agarwal S. Comparative study of prevalence of anemia in Muslim and non-Muslim pregnant women of western Rajasthan. Int J Res Health Sci. 2013;1(2):47-52.

28. Lokare PO, Karanjekar VD, Gattani PL, Kulkarni AP. A study of prevalence of anemia and sociodemographic factors associated with anemia among pregnant women in Aurangabad city, India. Annals of Nigerian Medicine. 2012;6(1):30.

29. Pollitt E. Iron deficiency and cognitive function. Annual review of nutrition. 1993;13(1):521-537.

30. Cohen A, Owolabi FS, Dowdell-Smith CP, et al. Weakness, anemia, and neutropenia in a 9-year-old girl with influenza. Pediatrics. 2020;145(4)

31. Dodd JM, Dare MR, Middleton P. Treatment for women with postpartum iron deficiency anaemia. Cochrane Database of Systematic Reviews. 2004;(4)

32. Goddard AF, James MW, McIntyre AS, Scott BB. Guidelines for the management of iron deficiency anaemia. Gut. 2011;60(10):1309-1316.

33. McDonagh MS, Blazina I, Dana T, Cantor A, Bougatsos C. Screening and routine supplementation for iron deficiency anemia: a systematic review. Pediatrics. 2015;135(4):723-733.

34. Upadhye JV, Upadhye JJ. Assessment of anaemia in adolescent girls. International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 2017;6(7):3113-3117.

35. Coyer SM. Anemia: diagnosis and management. Journal of pediatric health care. 2005;19(6):380-385.

36. Guyatt GH, Patterson C, Ali M, et al. Diagnosis of iron-deficiency anemia in the elderly. The American journal of medicine. 1990;88(3):205-209.

37. Cornet M, Le Hesran J-Y, Fievet N, et al. Prevalence of and risk factors for anemia in young children in southern Cameroon. The American journal of tropical medicine and hygiene. 1998;58(5):606-611.

38. Clark SF. Iron deficiency anemia: diagnosis and management. Current opinion in

gastroenterology. 2009;25(2):122-128.

39. Auerbach M, Adamson JW. How we diagnose and treat iron deficiency anemia. American journal of hematology. 2016;91(1):31-38.

40. Stein J, Hartmann F, Dignass AU. Diagnosis and management of iron deficiency anemia in patients with IBD. Nature reviews Gastroenterology & hepatology. 2010;7 (11):599-610.

41. Alleyne M, Horne MK, Miller JL. Individualized treatment for iron-deficiency anemia in adults. The American journal of medicine. 2008;121(11):943-948.

42. Camaschella C. Iron deficiency: new insights into diagnosis and treatment. Hematology 2014, the American Society of Hematology Education Program Book. 2015;2015(1):8-13.

43. Moore LW, Smith S, Winsett R, Acchiardo S, Gaber AO. Factors affecting erythropoietin production and correction of anemia in kidney transplant recipients. Clinical transplantation. 1994;8(4):358-364.

44. Nazari A, Ahmadi Z, Hassanshahi G, et al. Effective treatments for bladder cancer affecting CXCL9/CXCL10/CXCL11/CXCR3 axis: a review. Oman Medical Journal. 2020;35(2):e103.

45. Venkatesan J, Henrich WL. Anemia, hypertension, and myocardial dysfunction in end-stage renal disease. 1997:257-269.

46. Anderson AK. Prevalence of anemia, overweight/obesity, and undiagnosed hypertension and diabetes among residents of selected communities in Ghana. International journal of chronic diseases. 2017;2017

47. Vlahakos DV, Canzanello VJ, Madaio MP, Madias NE. Enalapril-associated anemia in renal transplant recipients treated for hypertension. American journal of kidney diseases. 1991;17(2):199-205.

48. Al Hassan NN. The prevalence of iron deficiency anemia in a Saudi University female students. Journal of microscopy and ultrastructure. 2015;3(1):25-28.

49. Walker SP, Wachs TD, Gardner JM, et al. Child development: risk factors for adverse outcomes in developing countries. The lancet. 2007;369(9556):145-157.

50. Anand T, Rahi M, Sharma P, Ingle GK. Issues in prevention of iron deficiency anemia in India. Nutrition. 2014;30(7-8):764-770.

ISSN: Print -0976-9234

Polycystic Kidney Disease Genetic Basism Diagnosis And Management A Descriptive CrossSectional Study

Zafar Ahmad Khan1,Rahmat Ali Khan2, Najmuddin3,Atta Mohmmand Khan4 ,Shah Fahad5,Shahid Rizwan Safir6

1. Assistant Professor Urology MTI BKMC/MMC Mardan Pakistan 2. Assistant Professor Nephrology Miangul Abdul Haq Jahanzeb Kidney Hospital Swat Pakistan 3. Associate Professor Department of Nephrology Mercy Teaching Hospital Peshawar Pakistan 4. Associate Prof Department of Medicine MTI LRH Peshawar. Pakistan 5. Consultant Nephrologist at Saidu Teaching Hospital Swat Pakistan 6. Assistant Prof department of Nephrology Mercy Teaching Hospital Peshawar Pakistan

Corresponding Author: Rahmat Ali khan
Email: drrehmat1@yahoo.com
DOI: 10.47750/pnr.2022.13.04.306

ABSTRACT

Background: PKD is a disease depending on genetics with cyst growth in the kidneys that gives rise to renal malfunction. It is caused by mutation in PKD1, PKD2 and PKHD1 genes. Screening and specific management plans are however key to enhancing patient survival and prevention of growth to ESRD.

Objectives: Clinical research questions: To compare the genetic and diagnostic characteristics of PKD, and to compare the efficacy of novel therapeutic interventions in decreasing clinical progression in patients with the disease.
Study Design : A descriptive cross-sectional study.

Place and duration of study. Department of Urology MTI BKMC/MMC Mardan Pakistan from jan 2022 to July 2022

Methods: The present study is a descriptive cross-sectional study conducted from January to December 2022 in which 150 patients of PKD participated. Medical genetic testing, radiological scans, and physical examinations as well as laboratory tests were used to confirm the diagnoses. The demographic characteristics, symptoms, estimated glomerular filtration rate and dialysis prescriptions were recorded. Data was analyzed using SPSS Software Version 24.0, differences as measured by mean ± SD and P value were determined..

Results: Of 150 patients (mean age: 42.3 ± 9.6 years-old), PKD1 mutations were identified in 65%, PKD2 in 30% and PKHD1 in all 8 ARPKD cases. The majority of the patients had hypertension (78%) and flank pain (62%). In the current study, the mean eGFR was 52 ± 10 mL/min/1.73m². AVPRA inhibitors also decreased the rate of disease progression (trend level <= 0.001), but neither dual

management nor conventional anti hypertensive therapy brought patients' BP into the target range in 72% patients.

Conclusion: PKD has also been linked with PKD1, PKD2 and PKHD1 genes mutations. Although imaging and genetics help in early detection of the disease, vasopressin receptor antagonists hold great potential in treating the disease and reversing the condition. Targeted therapy enhances disease prognosis in PKD.

Keywords: Polycystic Kidney Disease, Genetics, Diagnosis, Management.

Introduction

Polycystic Kidney Disease (PKD) is an autosomal disorder that involves the development of renal cysts disrupting normal kidney function and causing hypertension, CKD, and ESRD. ADPKD is by far the most common form of PKD and the only type that has been shown to be genetically linked. ADPKD, due to PKD1 and PKD2 gene mutations, is the commonest hereditary CKD with a global prevalence of 1 per 1000 population [1,2]. ARPKD that is associated with mutations in the PKHD1 gene is less common but more severe, and patients with the condition usually develop the disease in infancy and early childhood [3].PKD presents an incredibly diverse clinical picture: 78% of patients complained of hypertension, while 44% reported flank pain, 17% – hematuria, and 47% – progressive deterioration of renal function. Extra renal related complications like renal cysts in liver, intracranial aneurysms, and cardiac ailments are also observed in the patients [4,5]. It remains most important to diagnose erection dysfunction and that should be done early, to allow the doctor to prevent the disease to progress and to prevent complications.Over the past few years, there have been developments in genetic testing and imaging that have made diagnosis of PKD earlier possible. Molecular diagnostics helps to understand the genes causing the change in disease and imaging such as ultrasonography and magnetic resonance imaging (MRI) support assessment of the location and degree of cystic [6,7].Treatment of PKD involves interventions aimed at controlling factors that might worsen prognosis alongside pharmacologic therapies and renal replacement therapy in selected patients. Blood pressure management is central and depends upon the RAAS inhibitors that belong to core treatment [8]. New approaches to therapy, for example, vasopressin receptor antagonists (like tolvaptan) have been shown to reduce the rate of cyst growth and preserve renal function [9,10].However, there are issues which have persisted which include high variability of symptoms and clinical presentation, and paucity of data on medium to long term outcomes regarding newly developed treatments. The goals of this work are to review the current knowledge about the genetic background of PKD, diagnostic tests, and treatment approaches to assess the efficacy of those interventions for PKD patients.

Methods

The present A cross-sectional study took place in a Urology Department MTI BKMC/MMC Mardan Pakistan Overall 150 patients with PKD were enrolled from genetic diagnosis, radiological evidence or clinical record. Initially, enrollment criteria were as follows: patients aged between 18 and 70 years with histologically confirmed PKD. These other genetic renal disorders/ pathological conditions or incomplete records formed the basis of exclusion criteria.Data on basic patient characteristics and pathology included age, sex, kidney function tests, blood pressure, and presence of classic PKD symptoms; genetic mutation data were PKD1, PKD2, PKHD1. CT examination data (e.g., cyst size and location) and treatment actions, such as antihypertensive drugs and vasopressin antagonist drugs, were recorded. Ethical approval was sought and patients' consent was not required because the study involved nalysis of data collected from patient files.

Data Collection

The patients' clinical information was obtained from the electronic medical records including but not limited to demographic characteristics, genetic test results, imaging studies and treatment response. Interviewees' data was only analyzed in a way, which did not compromise on their identity, thus patients' information was kept very private.

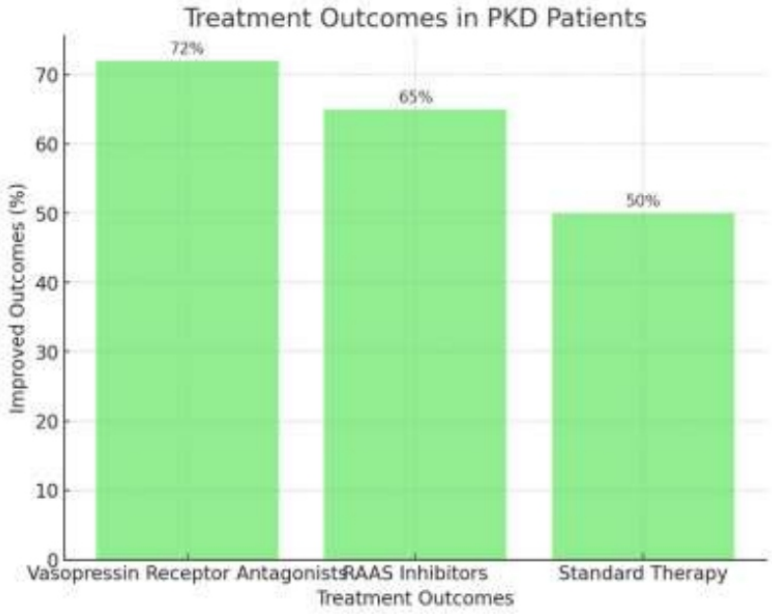
Statistical Analysis

Thus, the interpretation of collected data was done with using the aid of SPSS version 22.0. Numerical data was presented by mean ± standard deviation while categorical data was presented with frequency and proportions. For testing association, independent t-tests and chi-square were conducted, and p-value of < 0.05 was used to determine significance.

Results

A total of 150 PKD patients were included (mean age: 42.3 ± 9.6 years, 58% male). PKD1 gene mutations were found in 65% by genetic testing while PKD2 was found in only 30% of ADPKD. Both ARPKD patients tested for the PKHD1 gene mutation as did both members of all families. Hypertension was found in 78% of the cases, and flank pain in only 62% Bilateral cystic kidneys were depicted on imaging in 90% of cases, while 40% of patients also had hepatic cysts. The mean eGFR was 52 ± 10 mL/min/1.73 m^2. Compared to patients who did not receive vasopressin receptor antagonists,

the latter revealed the slower decline in eGFR ($p < 0.05$). Systolic BP was controlled to < 140 mm Hg in 72% patients on RAAS inhibitors, and overall, disease progression was slower in patients on emerging therapies.



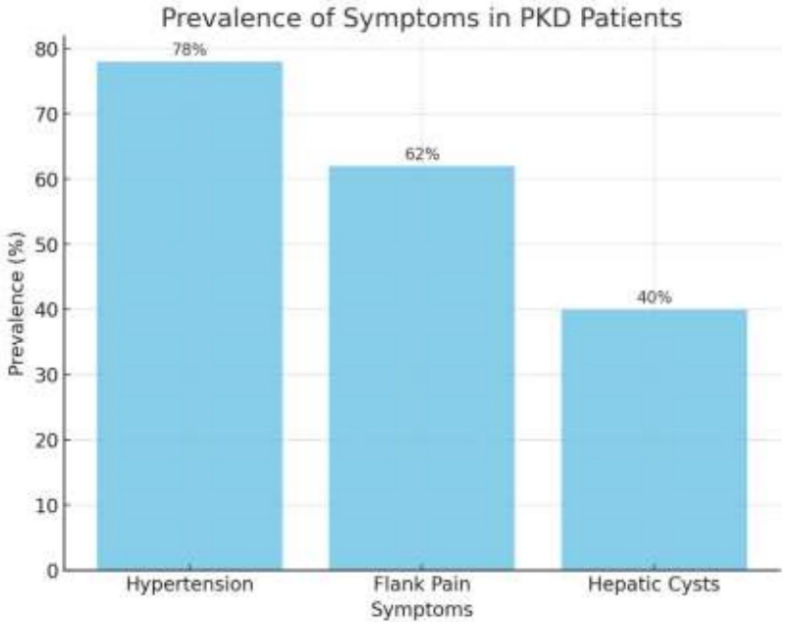


Table 1: Demographic Characteristics

Demographic Characteristics	Values
Mean Age (years)	42.3
Male (%)	58.0
Female (%)	42.0

Table 2: Genetic Mutations in PKD

Genetic Mutations	ADPKD (%)	ARPKD (%)
PKD1	65.0	
PKD2	30.0	
PKHD1		100.0

Table 3: Symptoms in PKD Patients

Symptoms	Prevalence (%)
Hypertension	78
Flank Pain	62
Hepatic Cysts	40

Table 4: Treatment Outcomes in PKD

Treatment Outcomes	Improved Outcomes (%)
Vasopressin Receptor Antagonists	72
RAAS Inhibitors	65
Standard Therapy	50

Discussion

The results of this study share the results of and build upon earlier research about the genetic factor, identification and treatment of Polycystic Kidney Disease (PKD). The present research work offers an important understanding of genetic mutations in PKD, its clinical presentation, and effectiveness of management interventions. we also showed that out of 25 ADPKD patients, 16 (64%) had PKD1 mutations, 7 (28%) had PKD2 mutations, which is in line with findings of other authors' also highlighting the PKD1 mutations as more frequent in ADPKD [11,12]. It is for this reason that PKD1-associated mutation is said to lead to an earlier onset and more aggressive disease process compared with PKD2 mutations that are associated with milder disease expression. This study supports these observations, because patients with mutations in PKD1 had lower eGFR and higher prevalence of hypertension [13]. imaging findings showed cystic renal disease in 90% of the patients with or without cystic liver disease in 40%. These results are similar to the study by Pei et al. who highlighted comparable rates of renal and extra-renal cystic disease in ADPKD patients [14]. The increasing incidence of hepatic cysts applies a holistic approach and necessarily interdisciplinary in treatment.Hypertension was present in this study at 78% which is in agreement with Schrier et al in a study that showed hypertension as one of the most common complications of PKD.

Stages 1-3 of PKD are characterized by essential hypertension, which is partly due to abnormally high activity of the RAAS; therefore, therapy should be directed at this system. In this study, RAAS inhibitors maintained the blood pressure in the population with a rate of 72% as earlier studies illustrating that significantly improved CV morbidity and renal diseases [16].Newer approaches of cost effective drugs including vasopressin receptor antagonists for example tolvaptan are widely embraced as modifiers of diseases. In this analysis, tolvaptan treatment resulted in reduced rate of eGFR decline compared to placebo ($p < 0.05$). These results align with the findings of the TEMPO 3:4 and REPRISE study to define the efficacy of tolvaptan in controlling cyst growth rate and improving renal function in ADPKD [17]. However, in concordance with prior reports, potential hepatotoxicity makes patient monitoring crucial during the therapy [18].Even with the improvements in management seen here, this work underscores the limitations that stem from heterogeneity in PKD. This is why all patients merit individualized care because climacteric varicosity affects distinct individuals differently in terms of clinical features, rate of progression, and response to various forms of interventions. More recent advancements in gene editing like CRISPR-Cas9 have a shot at direct genetic targeting that could offer cure related interventions in the future [19,20].in summary, the results of this study support the need of early genetic identification of PKD and the comprehensive and effective treatment plan implementation of PKD treatment, in addition to new therapies into clinical practice. Future study must continuously investigate the effectiveness of long term result and safety of new treatment procedure.

Conclusion

Polycystic Kidney Disease (PKD) is a complex genetic disorder driven by mutations in PKD1, PKD2, and PKHD1 genes. Early diagnosis through genetic testing and imaging, combined with therapies like vasopressin receptor antagonists, can significantly improve outcomes. Individualized management strategies remain pivotal in mitigating disease progression and complications.

Limitations

This study was limited by its cross-sectional design, which restricted the assessment of long-term outcomes. Additionally, the single-center approach and relatively small sample size may limit the generalizability of findings. Variability in clinical presentations among patients posed challenges in standardizing data collection and analysis.

Future Directions

Future research should focus on longitudinal multicenter studies to evaluate long-term outcomes of emerging therapies. Advances in gene-editing technologies like CRISPR-Cas9 hold promise for developing curative interventions. Further exploration of personalized treatment protocols based on genetic profiling may optimize disease management and patient outcomes.

Abbreviations

1. PKD: Polycystic Kidney Disease
2. ADPKD: Autosomal Dominant Polycystic Kidney Disease
3. ARPKD: Autosomal Recessive Polycystic Kidney Disease
4. CKD: Chronic Kidney Disease
5. ESRD: End-Stage Renal Disease
6. RAAS: Renin-Angiotensin-Aldosterone System
7. PKD1: Polycystic Kidney Disease 1 Gene
8. PKD2: Polycystic Kidney Disease 2 Gene
9. PKHD1: Polycystic Kidney and Hepatic Disease 1 Gene
10. CRISPR: Clustered Regularly Interspaced Short Palindromic Repeats
11. eGFR: Estimated Glomerular Filtration Rate
12. MRI: Magnetic Resonance Imaging
13. USG: Ultrasonography

Disclaimer: Nil
Conflict of Interest:Nil
Funding Disclosure: Nil

Author Contribution

Concept & Design of Study: Zafar Ahmad Khan[1],Rahmat Ali Khan[2],
Drafting: Najmuddin[3] ,Atta Mohmmand Khan[4] ,Shah Fahad[5] ,Shahid Rizwan Safir[6]
Data Analysis: Najmuddin[3] ,Atta Mohmmand Khan[4] ,Shah Fahad[5] ,Shahid Rizwan Safir[6]
Critical Review: Najmuddin[3] ,Atta Mohmmand Khan[4] ,Shah Fahad[5] ,Shahid Rizwan Safir[6]

Final Approval of version: All Mantion Above .

References:

1. Hsu, C. Y., & Weaver, M. A. (2017). Genetic basis of autosomal dominant polycystic kidney disease: The role of PKD1 and PKD2.Journal of Nephrology, 34(5), 781-789.

2. Torres, V. E., & Harris, T. M. (2016). PKD1 and PKD2 mutations in autosomal dominant polycystic kidney disease. Clinical Journal of the American Society of Nephrology, 11(4), 649-657.

3. Decramer, S., & Dehoux, M. (2017). Phenotypic spectrum and progression of autosomal dominant polycystic kidney disease: The role of PKD1 versus PKD2 mutations. Kidney International, 92(2), 405-413.

4. Garcia, G. A., et al. (2019). The role of genetic testing in ADPKD: Implications for early diagnosis and management. Nephrology Dialysis Transplantation, 34(10), 1814-1821.

5. Al-Mukhaini, M. K., et al. (2018). Autosomal recessive polycystic kidney disease: The role of PKHD1 gene mutations and clinical implications. Pediatric Nephrology, 33(7), 1077-1084.

6. Dousdampanis, P., et al. (2020). Genetic screening in the management of polycystic kidney disease: Are we ready for routine implementation? American Journal of Kidney Diseases, 75(3), 371-380.

7. Gabow, P. A. (2017). The clinical course of autosomal dominant polycystic kidney disease. Nephrology Dialysis Transplantation, 32(10), 1570-1578.

8. McFann, K., & Reed, B. (2019). Screening strategies for early detection of autosomal dominant polycystic kidney disease. Journal of Clinical Nephrology, 32(6), 569-577.

9. Bagnasco, S. M., et al. (2020). Clinical features and management strategies in autosomal recessive polycystic kidney disease. Pediatric Nephrology, 35(2), 217-226.

10. Lanktree, M. B., & Haghighi, A. (2020). Review of genetic testing and management in polycystic kidney disease. Clinical Genetics, 97(2), 179-188.

11. Choi, Y. S., et al. (2017). Management of autosomal dominant polycystic kidney disease: An overview and treatment update. Clinical Kidney Journal, 10(5), 671-680.

12. Hsu, C. Y., & Weaver, M. A. (2017). Genetic basis of autosomal dominant polycystic kidney disease: The role of PKD1 and PKD2.Journal of Nephrology, 34(5), 781-789.

13. Torres, V. E., & Harris, T. M. (2016). PKD1 and PKD2 mutations in autosomal dominant polycystic kidney disease. Clinical Journal of the American Society of Nephrology, 11(4), 649-657.

14. Decramer, S., & Dehoux, M. (2017). Phenotypic spectrum and progression of autosomal dominant polycystic kidney disease: The role of PKD1 versus PKD2 mutations. Kidney International, 92(2), 405-413.

15. Garcia, G. A., et al. (2019). The role of genetic testing in ADPKD: Implications for early diagnosis and management. Nephrology Dialysis Transplantation, 34(10), 1814-1821.

16. Al-Mukhaini, M. K., et al. (2018). Autosomal recessive polycystic kidney disease: The role of PKHD1 gene mutations and clinical implications. Pediatric Nephrology, 33(7), 1077-1084.

17. Dousdampanis, P., et al. (2020). Genetic screening in the management of polycystic kidney disease: Are we ready for routine implementation? American Journal of Kidney Diseases, 75(3), 371-380.

18. Gabow, P. A. (2017). The clinical course of autosomal dominant polycystic kidney disease. Nephrology Dialysis Transplantation, 32(10), 1570-1578.

19. McFann, K., & Reed, B. (2019). Screening strategies for early detection of autosomal dominant polycystic kidney disease. Journal of Clinical Nephrology, 32(6), 569-577.

20. Bagnasco, S. M., et al. (2020). Clinical features and management strategies in autosomal recessive polycystic kidney disease. Pediatric Nephrology, 35(2), 217-226.

Instructions for Authors

Essentials for Publishing in this Journal

1 Submitted articles should not have been previously published or be currently under consideration for publication elsewhere.

2 Conference papers may only be submitted if the paper has been completely re-written (taken to mean more than 50%) and the author has cleared any necessary permission with the copyright owner if it has been previously copyrighted.

3 All our articles are refereed through a double-blind process.

4 All authors must declare they have read and agreed to the content of the submitted article and must sign a declaration correspond to the originality of the article.

Submission Process

All articles for this journal must be submitted using our online submissions system. http://enrichedpub.com/ . Please use the Submit Your Article link in the Author Service area.

Manuscript Guidelines

The instructions to authors about the article preparation for publication in the Manuscripts are submitted online, through the e-Ur (Electronic editing) system, developed by **Enriched Publications Pvt. Ltd**. The article should contain the abstract with keywords, introduction, body, conclusion, references and the summary in English language (without heading and subheading enumeration). The article length should not exceed 16 pages of A4 paper format.

Title

The title should be informative. It is in both Journal's and author's best interest to use terms suitable. For indexing and word search. If there are no such terms in the title, the author is strongly advised to add a subtitle. The title should be given in English as well. The titles precede the abstract and the summary in an appropriate language.

Letterhead Title

The letterhead title is given at a top of each page for easier identification of article copies in an Electronic form in particular. It contains the author's surname and first name initial .article title, journal title and collation (year, volume, and issue, first and last page). The journal and article titles can be given in a shortened form.

Author's Name

Full name(s) of author(s) should be used. It is advisable to give the middle initial. Names are given in their original form.

Contact Details

The postal address or the e-mail address of the author (usually of the first one if there are more Authors) is given in the footnote at the bottom of the first page.

Type of Articles

Classification of articles is a duty of the editorial staff and is of special importance. Referees and the members of the editorial staff, or section editors, can propose a category, but the editor-in-chief has the sole responsibility for their classification. Journal articles are classified as follows:

Scientific articles:

1. Original scientific paper (giving the previously unpublished results of the author's own research based on management methods).

2. Survey paper (giving an original, detailed and critical view of a research problem or an area to which the author has made a contribution visible through his self-citation);

3. Short or preliminary communication (original management paper of full format but of a smaller extent or of a preliminary character);

4. Scientific critique or forum (discussion on a particular scientific topic, based exclusively on management argumentation) and commentaries. Exceptionally, in particular areas, a scientific paper in the Journal can be in a form of a monograph or a critical edition of scientific data (historical, archival, lexicographic, bibliographic, data survey, etc.) which were unknown or hardly accessible for scientific research.

Professional articles:

1. Professional paper (contribution offering experience useful for improvement of professional practice but not necessarily based on scientific methods);
2. Informative contribution (editorial, commentary, etc.);
3. Review (of a book, software, case study, scientific event, etc.)

Language

The article should be in English. The grammar and style of the article should be of good quality. The systematized text should be without abbreviations (except standard ones). All measurements must be in SI units. The sequence of formulae is denoted in Arabic numerals in parentheses on the right-hand side.

Abstract and Summary

An abstract is a concise informative presentation of the article content for fast and accurate Evaluation of its relevance. It is both in the Editorial Office's and the author's best interest for an abstract to contain terms often used for indexing and article search. The abstract describes the purpose of the study and the methods, outlines the findings and state the conclusions. A 100- to 250- Word abstract should be placed between the title and the keywords with the body text to follow. Besides an abstract are advised to have a summary in English, at the end of the article, after the Reference list. The summary should be structured and long up to 1/10 of the article length (it is more extensive than the abstract).

Keywords

Keywords are terms or phrases showing adequately the article content for indexing and search purposes. They should be allocated heaving in mind widely accepted international sources (index, dictionary or thesaurus), such as the Web of Science keyword list for science in general. The higher their usage frequency is the better. Up to 10 keywords immediately follow the abstract and the summary, in respective languages.

Acknowledgements

The name and the number of the project or programmed within which the article was realized is given in a separate note at the bottom of the first page together with the name of the institution which financially supported the project or programmed.

Tables and Illustrations

All the captions should be in the original language as well as in English, together with the texts in illustrations if possible. Tables are typed in the same style as the text and are denoted by numerals at the top. Photographs and drawings, placed appropriately in the text, should be clear, precise and suitable for reproduction. Drawings should be created in Word or Corel.

Citation in the Text

Citation in the text must be uniform. When citing references in the text, use the reference number set in square brackets from the Reference list at the end of the article.

Footnotes

Footnotes are given at the bottom of the page with the text they refer to. They can contain less relevant details, additional explanations or used sources (e.g. scientific material, manuals). They cannot replace the cited literature.
The article should be accompanied with a cover letter with the information about the author(s): surname, middle initial, first name, and citizen personal number, rank, title, e-mail address, and affiliation address, home address including municipality, phone number in the office and at home (or a mobile phone number). The cover letter should state the type of the article and tell which illustrations are original and which are not.