

Quality of Life

(Banja Luka)

Izdavač/Published by Panevropski univerzitet "Apeiron" Banja Luka/ Pan-European University "Apeiron" Banja Luka
Urednik izdavača/Editor of University Publications Aleksandra Vidović, Bosnia and Herzegovina

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Technical Editor/Layout Sretko Bojić
Web design Marko Milovanović
Printed by Markos design & print studio, Banja Luka
Printed in 300 copies

Aim and Scope

Quality of Life publishes original research papers and reviews and aims to provide a forum for the rapid dissemination of significant novel research in the various disciplines encompassing the Science and technology of food, Public health engineering, Sanitary inspection and control, Environmental and public health. Topics covered by the journal include:

- Dietetics; Nutrition principles applied to foods
- Food Technology; Production and preservation of foodstuffs; Food preservation technique
- Industrial microbiology; Science and technique of applied microbiology; Applied mycology
- Public Health, environment and hygiene
- Hygiene of air, water, soil; Pollution and its control
- Water; Sanitation; Water treatment
- Sewage; Treatment, disposal, utilization of sewage
- Urban hygiene; Wastes; Refuse; Rubbish; Garbage; Collection and disposal of town wastes
- Measures against industrial and other nuisances
- Occupational health hazards; Occupational health and hygiene
- Ecology; Environmental engineering, sustainability and health
- Related topics

UDC 614 Quality of Life is registered with the Ministry of Science and Technology of the Republic of Srpska by serial registration code 07.030-053-160-4/10, date 03.03.2010.
Quality of Life (ISSN 1986-602X) is an international journal published two times a year.

Indexed in:

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 citefactor.org/contact

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 doisrpska.nub.rs

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DEAR READERS AND AUTHORS,

As Editor-in-Chief of the journal Quality of Life, I look forward to the challenge of creating a journal that will enhance the quality of research in the various disciplines encompassing the Science and technology of food, Public health engineering, Sanitary inspection and control, Environmental and public health in our country, the region as well as at the international level. The journal Quality of Life was registered in the Register of Public Media in 2010 by the Decision of the RS Ministry of Education and Culture. Over the past years, this journal has published a large number of original scientific research papers, communications and review papers. Quality of Life is published twice a year by Pan-European University "Apeiron" Banja Luka. All the papers published so far have undergone a thorough review by the editorial board and the reviewers, made up of experts from both RS/B&H, the surrounding and other countries, from proven and recognized university and research institutions. As a result of a professional approach to selecting and reviewing papers, and raising the quality of the journal, Quality of Life was classified in the first category of journals in 2019 by the Ministry of Education and Culture.

We are proud to say that Quality of Life has been well received by the scientific and the general public in a relatively short period, which gives the editorial board a strong motivation for further work. The editorial team would like to thank our many reviewers who helped to maintain the journal standard; our many authors who submitted their best work to the journal; and, most importantly, our readers for your continuing support. I shall assure all our readers that our consistent efforts will be aimed toward increasing the visibility, impact, editorial cycle time, citations and overall quality of our journals. We very much look forward to strengthening the reputation of our publications, and we want to attract more higher-quality submissions.

In the spirit of continuous improvement, any constructive input on streamlining our processes is very welcome. Please help us grow by citing articles that you read in Quality of Life. We look forward to receiving your contributions in the near future.

Editors

DOI: 10.7251/QOL2303093I

UDC: 546.18:547.314.2

Original scientific paper

ACCIDENTAL RELEASES OF TOXIC GAS ACETYLENE-SIMULATION WITH ALOHA SOFTWARE

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ABSTRACT: Uncontrolled acetylene release during production processes, transportation, or storage can lead to explosions and detonations endangering safety of people and material assets. This paper investigates the impact of accidental release of acetylene gas in surrounding areas. The ALOHA software has been used in this paper to modelling of acetylene release. The modelling was performed for an accidental release of 2,000 kg acetylene from direct source for one minute. For a typical average atmospheric condition in location, this accidental acetylene release would cause a red zone of 197 m (15,000 ppm) and yellow zone of 483 m (2,500 ppm) to downwind from the source. Inadequate storage can lead to accidental situations and negative impact on people and the environment.

Keywords: air pollution, ALOHA, acetylene, modelling.

INTRODUCTION

In the recent years, world has seen a wide range of major accidents with a number of fatalities, economic losses, and damage to the environment. These accidents can lead to serious danger to human health and the environment, which can occur inside or outside the establishment (Ilić et al., 2018). The chemical industry is one of the major potential environmental polluters. The release of any chemical may lead to toxic effects, fire, and explosion, and it makes the activity critical for safety systems to be made efficient and adequate to mitigate the haphazard in case of emergency. (Yadav et al., 2022). A great variety of its negative impacts affect both living organisms and material assets. Particularly dangerous are industrial sites, where emergencies are possible with the sudden formation of intense, diverse impact factors (shock waves, heat waves, emission of toxic substances). In this case, it is extremely important to predict the risk of damage to personnel in the workplace during emergencies (Biliaiev et al., 2020a).

According to European Union Directive–Seveso II, a chemical accident is defined as a result of unplanned and unpredicted events in the course of industrial activity being manifested through the emission of toxic substances in the environment or through fire or explosion. The accidents comprising one or more hazardous chemicals jeopardize humans and the environment both immediately or with delay, inside or outside the installation (Komatina et al., 2018). In addition to the proven impact on humans, the impact on

plant life has also been confirmed (Ilić and Maksimović, 2011). Improper handling and accidental release of hazardous chemicals pose serious public health hazards. The intensity of such accidents depends on the nature of the release, toxicity of the material, population density, and meteorological factors (Ilić et al., 2019). The above can cause air pollution, which represents a significant risk to the health of the population (Ilić, 2015; Ilić et al., 2018, 2019, 2020; Radović et al., 2022; Ćirišan et al., 2023). In case of emergencies, it is very important to assess the risk of damage to people (Biliaiev et al., 2020b).

Acetylene (C_2H_2) is the simplest hydrocarbon (Pässler et al., 2000). It is the unsaturated hydrocarbon belonging to the alkyne group. Its molecule is linear and built up from two carbon atoms bonded together in a triple bond. One hydrogen atom is bonded to every carbon atom (Komatina et al., 2018). Before oil became the main feedstock of the chemical industry, acetylene was the predominant building block of industrial organic chemistry (Pässler et al., 2000). Pure acetylene is colorless, odorless, and tasteless at normal temperature and pressure. At higher temperatures and under higher pressures, acetylene decomposes spontaneously, releasing a large quantity of energy and causing chain reactions that result in explosion. Uncontrolled acetylene release during production processes, transportation, or storage can lead to explosions and detonations, endangering the safety of people and material assets (Komatina et al., 2018). Pässler et al. (2000) provided information on some basic physical properties of acetylene. Acetylene has a molecular mass of 26.0379. Its critical temperature is reported as 308.32 K (35.17 °C), and its critical pressure is 6.139 MPa. The critical volume of acetylene is 0.113 m³/kmol. The triple point of acetylene occurs at 192.4 K (80.75 °C), and its corresponding pressure is 128.3 kPa. The normal sublimation point of acetylene is 189.15 K (4.0 °C). Acetylene also has a crystal transition point at 133.0 K (140.15 °C), and its enthalpy of transition is 2.54 kJ/mol.

This paper investigates the impact of the accidental release of acetylene gas in surrounding areas. The aim of this paper is to point out the inadequate storage and handling of acetylene, i.e. the consequences for human health and the environment.

MATERIALS AND METHOD

LOCATION AND ACETYLENE STATION

The subject of the research is the impact of the accidental release of acetylene gas in the business zone “Ramići-Banja Luka”, Banja Luka (Figure 1). Banja Luka is a city in the Republic of Srpska, Bosnia and Herzegovina (B&H). Banja Luka is located in Vrbas valley and is surrounded by hills 200-600 meters above sea level high. Banja Luka is the second biggest city in B&H, with a population of 200,000. Situated in a basin 164 m above sea level, where the Dinaric Alps from the south descend into the Pannonian Basin in the north.

Acetylene station is about 200 m away from the first residential building, north (Figure 1).



Figure 1. Position and distance of station from the first residential object (Google Earth)

Banja Luka has a temperate continental climate with prevailing influences from the Pannonian plain. It belongs to the Central European Time zone (GMT +1). The average annual temperature reaches 10.7°C, the average temperature in January reaches 0.8°C, whereas the average temperature in July reaches 21.3°C.

SOFTWARE ANALYSIS

Numerical models may be considered from two perspectives: first, as operational models applied by decision-makers where results should be clear and instantly available, and second, as models where simulation time is less important, and more importance is given to the accuracy of results and the most thorough consideration of the complexity of phenomena. There are various parameters and criteria for assessing the impacts of the toxicity of chemical materials. Losses and damages caused by the release and spread of toxic chemicals depend on the concentration of the toxic chemical and its contact time. In order to conduct incident modelling, ALOHA software (Areal Location of Hazardous Atmosphere) Version 5.4.7 was used (Ruhipour et al., 2017). ALOHA is the hazard-modelling program for the CAMEO (Computer-Aided Management of Emergency Operations) software suite, which is widely used to plan for and respond to chemical emergencies. ALOHA allows the user to choose from several accident scenarios and then uses an appropriate source algorithm to inject material into the air over a limited time. The source emission time may vary between limits of one minute to one hour. A flat, homogeneous Earth is assumed. For the purposes of solar radiation and day/night decisions, time is fixed at the moment the leak begins. ALOHA can model toxic gas clouds, flammable gas clouds, Boiling Liquid Expanding Vapor Explosions (BLEVEs), jet fires, pool fires, and vapor cloud explosions. The threat zone estimates are shown on a grid in ALOHA and can also be plotted on maps in MARPLOT, Esri's ArcMap, Google Earth, and Google Maps. The red threat zone represents the worst hazard level, and the orange and yellow threat zones represent areas of decreasing hazard (www.epa.gov/cameo/aloha-software; Ilić et al., 2018; Joseph & Williams, 2022).

To model hazards using ALOHA, several required inputs are entered into the software. These inputs include basic scenario information such as the date, time, and location of the event. A chemical is chosen from ALOHA's chemical library, and atmospheric information, including wind speed and direction, air temperature, and cloud cover, is entered either manually or automatically using a portable station for at-

mospheric measurements (SAM). Additionally, a source is chosen from options such as direct, puddle, gas pipeline, or tank, and corresponding source information, including release amount, tank dimensions, and whether the chemical is burning, is entered. The Levels of Concern (LOCs) to be used for estimating the threat zones are specified, or default LOCs offered by ALOHA are used. Furthermore, the type of hazard, such as toxicity or thermal radiation, to be used when estimating the threat zones is also chosen. The entered data for acetylene in ALOHA is presented in Figure 2.

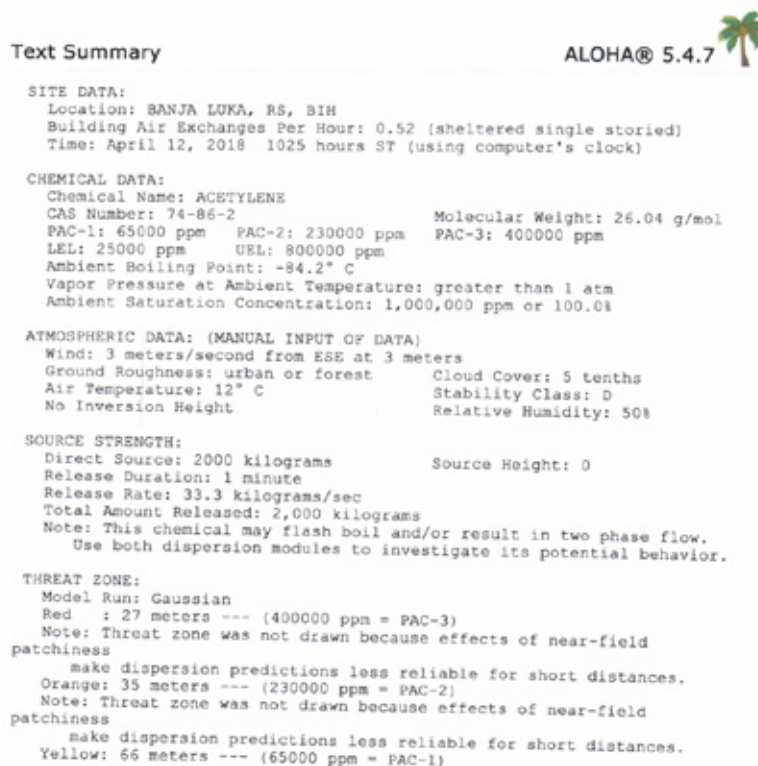


Figure 2. Entered data in software for acetylene

The rate at which a chemical becomes airborne is critical for determining the size and duration of a toxic or flammable cloud. ALOHA utilizes a range of models known as source strength models to estimate the rate at which a chemical is released from containment and enters the atmosphere (Jones et al., 2013). For this study, a direct source model was employed, involving the instantaneous or continuous release of chemical vapors into the air from a single point. This option is the only one that permits an elevated release.

With the direct source option in ALOHA, the user can specify the amount of chemical vapors introduced into the air from a specific point in space. The user can select between an instantaneous or steady-state release of finite duration. This option is appropriate for gases that are denser than air and are affected by gravity or gases that behave as neutrally buoyant. ALOHA allows for a release above ground level for gases that behave as neutrally buoyant (Jones et al., 2013). The source emission time may vary between limits of one minute to one hour (Bhattacharya & Ganesh Kumar, 2015). For this study, the direct source option was used for one minute.

ALOHA employs a graphical interface to display the results and for data entry. Threat zones, which depict the area within which there is a potential for exposure to toxic vapors, a flammable atmosphere, over-pressure from a vapor cloud explosion, or thermal radiation from a fire, are represented graphically. These threat zones indicate the area where ground-level exposure exceeds the user-specified level of concern at some time after the release. All points within the threat zone experience a transient exposure exceeding the

level of concern at some point following the release, serving as a record of the anticipated peak exposure over time. In certain scenarios, the user may also view the time dependence of the exposure at specific points (Jones et al., 2013).

For the accidental release of 2,000 kg of acetylene, modeling was performed. The accident simulation was positioned in accordance with the entered coordinates (44°84'19.80"N 17°17'85.34"E) and can be rotated to face the direction of the wind that blows at a certain point.

RESULTS AND DISCUSSION

MODELLING THE EFFECTS OF ACETYLENE RELEASE AND SPREAD - TOXIC EFFECT

For a typical average atmospheric condition at this location, iso-concentration lines of toxic zones based on the gas model have been calculated, and the following zones have been obtained: the red zone (27 m, 400,000 ppm = PAC-3) and the orange zone (35 m, 230,000 ppm = PAC-2) are not plotted because the prediction dispersion is less reliable for short distances, and the yellow zone (66 m, 65,000 ppm = PAC-1).

As the gas moves towards the limits of the vulnerable zones, it creates a toxic effect that can be life-threatening. Workers who are in the yellow zone (Figure 3) may experience serious health effects or symptoms that can weaken their ability to take protective measures.

Protective Action Criteria (PACs) are essential components for planning and responding to uncontrolled releases of hazardous chemicals. These criteria, in combination with exposure estimates, provide the necessary information to evaluate chemical release events and take appropriate protective actions. During an emergency response, PACs may be used to evaluate the severity of the event, identify potential outcomes, and decide what protective actions to take (Protective, 2012).

The PACs dataset is a hierarchy-based system of the three most common public exposure guideline systems: Acute Exposure Guideline Levels (AEGLs), Emergency Response Planning Guidelines (ERPGs), and Temporary Emergency Exposure Limits (TEELs). AEGLs are established by the U.S. Environmental Protection Agency (EPA) and represent threshold concentrations of a substance in the air that can cause adverse health effects, such as respiratory or neurological impairment, to individuals exposed to it for a short period of time (up to 8 hours). ERPGs are developed by the American Industrial Hygiene Association (AIHA) and represent airborne concentrations of a substance above which an emergency response plan should be implemented to protect workers and the public. TEELs are established by the U.S. Department of Energy (DOE) and represent threshold concentrations of a substance in the air that can cause immediate and irreversible health effects, such as severe respiratory distress or death, to individuals exposed to it for a short period of time (up to 30 minutes) (Acute Exposure Guideline, 2018).

The PACs dataset uses a hierarchy-based system when choosing which values to use for the PACs of a hazardous substance. The preferred values are the Final, 60-minute AEGL values, followed by the Interim, 60-minute AEGL values. If those values are not available, the dataset uses the ERPG values, and if those are not available either, it uses the TEEL values.

The PACs dataset provides a set of values (PAC-1, PAC-2, and PAC-3) for each chemical, but the source of those values may vary. For instance, the PAC-3 value for one chemical may be an ERPG-3, while for a different chemical, it may be the TEEL-3. A hierarchical system is useful for selecting levels of concern for chemicals that are defined under two or more public exposure guidelines. In Aloha, PAC-1, PAC-2, and PAC-3 values can be selected to estimate threat zones. The yellow, orange, and red zones indicate areas where these values are predicted to be exceeded after the release of the chemical. For acetylene, ALOHA provides the PAC values as the default toxic LOCs until AEGL or ERPG values are established.

There are three levels of PAC value, with each level indicating a higher level of exposure and an increasingly severe effect. The levels are PAC-1, PAC-2, and PAC-3, with PAC-1 associated with mild, transient health effects, PAC-2 associated with irreversible or other serious health effects that could impair the ability to take protective action, and PAC-3 associated with life-threatening health effects (Protective, 2012).

Table 1. PACs (Protective Action Criteria) (<https://cameochemicals.noaa.gov/chemical/18>)

Chemical	PAC-1	PAC-2	PAC-3	
Acetylene (74-86-2)	65,000 ppm 🔥🔥🔥	230,000 ppm 🔥🔥🔥	400,000 ppm 🔥🔥🔥	LEL = 25,000 ppm

🔥🔥🔥 indicates value is 100% or more of LEL.

Figure 3 shows the threat zone in case of accidental release of acetylene.

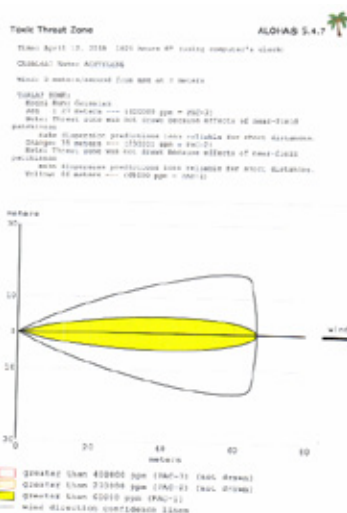


Figure 3. Toxic threat zone of release and spread of toxic effect-acetylene

Table 2. PACs values for Acetylene in ppm (https://sp.eota.energy.gov/pac/docs/Revision_29_Table2.pdf)

PACs based on AEGLs, ERPGs, or TEELs		
PAC-1	PAC-2	PAC-3
65,000*	230,000*	400,000*

* indicates PAC ≥ LEL

MODELING THE EFFECT OF THE POSSIBILITY OF IGNITING A VAPOR CLOUD OF A DANGEROUS SUBSTANCE - ACETYLENE

According to the results obtained from the calculation of the vulnerable zone using the heavy gas model, the flammable zones for acetylene are represented by two iso-concentration lines. The first line is the red zone, which covers an area of 197 m and is characterized by a concentration of 15,000 ppm (parts per million) of acetylene, equivalent to 60% of the lower explosive limit (LEL). The second line is the yellow zone, which covers an area of 483 m and is characterized by a concentration of 2,500 ppm of acetylene, equivalent to 10% of LEL. It is important to note that the LEL is defined as the lowest concentration (percentage) of a gas or vapor in air that is capable of producing a flash of fire in the presence of an ignition

source. Safety professionals often consider it to be the same as the lower flammable limit (LFL). If concentrations of a flammable gas or steam are greater than 10%, evacuation of the area should be carried out as a precautionary measure.

The red zone includes a portion of the business zone, while the yellow zone covers both the population and a portion of the business zone (as shown in Figure 4).

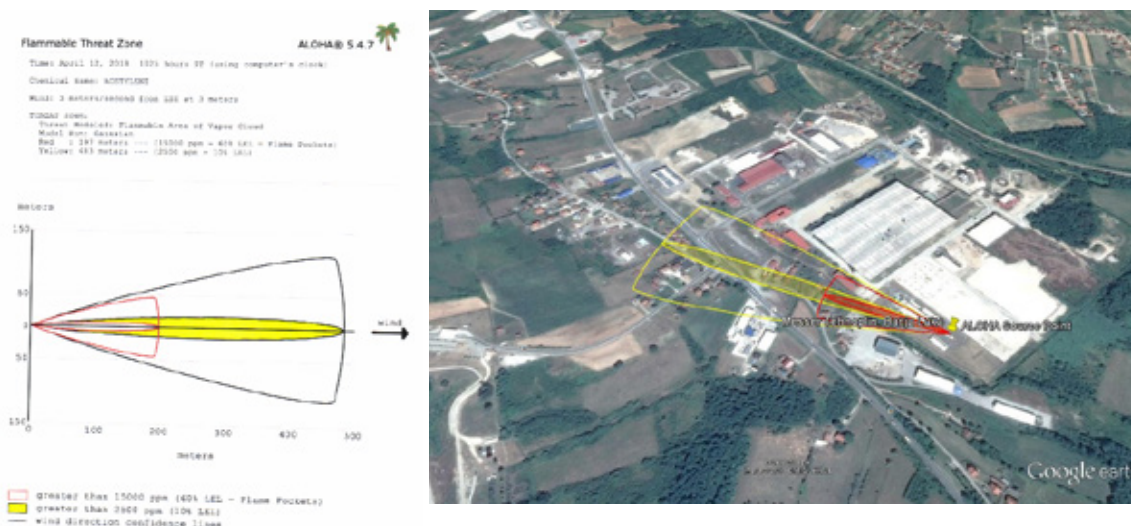


Figure 4. Iso-concentration lines of flammable zones and possible development of events - scenario of the possibility of ignition of a vapor cloud of dangerous substance - acetylene

MODELLING THE EFFECTS OF A VAPOR CLOUD EXPLOSION - ACETYLENE

ALOHA characterizes the damaging effect of the blast wave by using only the pressure peak. The blast wave can cause damage directly to pressure-sensitive organs, such as the ears and lungs, or indirectly, by accelerating debris or causing building collapse. ALOHA uses three levels of concern (LOCs) to quantify the direct and indirect effects. Glass windows can break at a pressure of 1 psi, at 3.5 psi there is a significant risk of ear and lung damage and injury from flying debris, and at 8 psi there is a significant risk of unreinforced building collapse, ear and lung damage.

The vulnerable zone is calculated based on the gas model and shock wave model, which considers the explosion of a gas cloud caused by a spark or flame. Isolines of overpressure from the center of the explosion are obtained, with the red zone representing areas where pressure is greater than 8 psi, causing damage to equipment and buildings. The orange zone (3.5 psi) represents a risk of serious injury, and the yellow zone (1.0 psi) is where glass windows could break, with a range of 174 m.

There are no accurate data on the number of employees per vulnerable zone. It is estimated that the total number of employees in the business zone is around 6,000. The population of Ramići is 2,105.

Figure 5 shows the overpressure due to an acetylene explosion and examples of steam cloud effects for acetylene.



Figure 5. Over-pressure due to Acetylene Explosion and Examples of scenario Steam Cloud effects for acetylene

CONCLUSION

The use of ALOHA software provides decision-makers with an effective tool for modeling the release of hazardous chemicals and estimating the potential impacts. The direct source model option in ALOHA allows for an elevated release and enables the user to specify the amount of chemical vapors introduced into the air from a particular point in space. The threat zones, which represent the area within which there is a possibility of exposure to toxic vapors or a flammable atmosphere, were represented graphically using ALOHA’s graphical interface.

Acetylene is a highly flammable and explosive gas, and it poses significant dangers to the environment. Simulation of acetylene release scenarios indicates a high risk of fire and explosion, which could significantly endanger the working environment and the area around the “Ramići” business zone in Banja Luka. According to ALOHA software, damage may occur due to direct or indirect effects of the pressure shock wave. Direct effects may include damage to pressure-sensitive organs such as the ears and lungs. Indirect effects may result from glass fragments from broken windows, collapsing buildings, or debris accelerated by the blast wave. ALOHA includes three LOCs that quantify indirect and direct effects. Glass windows can break at a pressure of 1 psi; at 3.5 psi, there is a significant risk of eardrum injury and injury from flying debris; at 8 psi, there is a significant risk of ear and lung damage, as well as an indirect effect from the collapse of unreinforced buildings.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Received: March 17, 2023

Accepted: May 25, 2023



DOI: 10.7251/QOL2303102L

UDC: 618.2612.015.6]:577.161.1

Original scientific paper

RESEARCH OF THE VASCULAR ENDOTHELIAL GROWTH FACTOR EXPRESSION IN THE PLACENTA

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ABSTRACT: Introduction: The development of tissues in certain organs takes place simultaneously with the development of blood vessels. The placenta is an organ whose development provides a unique model for examining and understanding the process of organogenesis. The vascular endothelial growth factor (VEGF) is one of the first identified angiogenic factors and one of the most important regulators of normal and pathological angiogenesis. The aim of the study was to determine the localization and intensity of VEGF expression in the normal term placenta. Methods: The study analyzed ten normal term placental samples of healthy pregnant women (from the 38th to the 40th week of gestation). Placental tissue sections were stained with the standard hematoxylin-eosin method (HE) and with the immunohistochemical method for VEGF. Results: The small number of cells of the amniotic epithelium and trophoblast had positive VEGF expression of low intensity. Positive VEGF expression of moderate intensity was present in a small number of cells of the chorionic plate stroma, villi stroma, and basal plate. Positive VEGF expression of moderate intensity was present in more than 50% of endothelial cells (3+) of all placental blood vessels. Conclusions: Positive VEGF expression was present in the amniotic epithelium, mesenchymal cells of the chorionic plate, trophoblast, stroma cells of the villi, endothelial cells of the placental blood vessels, and the cells of the basal decidua. In the placenta, the most intensive immunoreactivity for VEGF was present in the endothelium of the placental blood vessels. Positive VEGF expression in the normal placenta indicates a significant role of VEGF in the development of the placenta.

Keywords: placenta, vascular endothelial growth factor A, immunohistochemistry.

INTRODUCTION

Placental angiogenesis is a key process for the development of the placenta, as well as for the development of all other tissues (Ortega et al, 2022). Angiogenesis is a process in which budding, lateral growth and branching of new blood vessels occur from preexisting blood vessels. The development of tissues in certain organs, such as the development of the retina of the eye, takes place simultaneously with the development of blood vessels. The organ whose development provides a unique model for examining and understanding the process of organogenesis is the placenta (Clark et al, 1988). The placenta is a temporary organ for the growth and development of the fetus that ensures the transfer of nutrients from the mother's organism. This discoid-shaped organ is the only source of oxygen and nutrients for the fetus. The specificity of the placenta as an organ lies in the complexity and extent of its functions, and its limited duration. The placenta lasts as long as the pregnancy lasts (Draganović, 2020).

Disorders such as pregnancy-induced hypertension (PIH) and intrauterine growth restriction (IUGR), which may not become obvious until the third trimester of pregnancy, are thought to be the result

of inadequate placentation in early pregnancy (Kaufmann, 2003). The pathogenesis of PIH is explained by hypoperfusion and ischemia of the placenta resulting from the failure in remodeling of spiral arterioles in the decidua. Analyses of the placenta in IUGR indicate inadequate angiogenesis in the placenta, reduced vascularization of the terminal villi of the placenta, and reduced maternal and fetal blood flow (Warrander et al, 2012; Draganovic et al, 2021; Ljubojević et al, 2022, Jovičić et al 2020). VEGF is one of the first identified angiogenic factors and one of the most important regulators of normal and pathological angiogenesis (Helske et al, 2001; Wu et al, 2023). During pregnancy, VEGF participates in the proliferation, migration, and metabolic activity of trophoblasts and plays a key role in the formation of new blood vessels. During placental development, VEGF has a dual role in the placenta acting on both angiogenesis and trophoblast function. The aim of the study was to determine the localization and intensity of VEGF expression in the normal term placenta.

METHODS

The study analyzed ten normal-term placental samples of healthy pregnant women. The gestation of the pregnant women was from the 38th to the 40th week of gestation. The study was performed at the university setting of the University of Banja Luka, Faculty of Medicine. The study was approved by The Ethics Committee of the University Clinical Center of Republic Srpska in Banja Luka and it was conducted in accordance with the Declaration of Helsinki. The collected placentas for histological analysis were without noticeable macroscopic damage and alterations. The placental tissue samples, size 1x1 cm were dissected at a medium distance from the center and margin of the placenta. The samples include whole-thickness of the placenta, from the basal to the chorionic plate. After fixation in 10% neutral buffered formalin, the tissues were processed and then embedded in paraffin wax. For histological analysis 5 µm thick tissue sections were obtained, and they were stained with the standard hematoxylin-eosin method and with the immunohistochemical staining method using anti-VEGF antibody (Dako). Antigen retrieval was performed for 20 min in citrate buffer at pH 6.0. For blocking endogenous peroxidase activity the tissue sections were incubated with a 3% hydrogen peroxide solution for 5 minutes at room temperature. Then, the sections were washed briefly with distilled water and after that with phosphate-buffer saline (PBS) for five minutes (Dako, EnVSION FLEX WASH BUFFER). Incubation with primary antibody (monoclonal ab-VEGF, clone VG1, 1:25 and 1:50) was performed for 30 minutes at room temperature. Afterward, the sections were washed three times for three minutes in PBS and reincubated with HRP polymer anti-mouse (Dako K4000) for 30 min. After washing in PBS the sections were treated with 3,3'-diaminobenzidine (DAB) chromogen was used and the reaction was monitored under a microscope. The counterstaining with Mayer hematoxylin was performed also.

All placental tissues in the placental sample were evaluated for VEGF immunoreactivity. The intensity of staining was classified into four categories: 0 - negative, 1 - weak, 2 - moderate, and 3 - strong. Depending on the percentage of immunopositive cells immunoreactivity was divided into five categories: 0 = all cells were negative; 1+ = from 0 to 25% of cells were positive; 2+ = if 25 – 49% of cells were positive; 3+ = if 50 – 75% of cells were positive; and 4+ = if >75% of cells were positive (Schuessl et al, 2009). VEGF expression in blood vessels of placental samples was estimated as positive if VEGF immunoreaction was present in endothelial cells in 10% or more blood vessels of the placenta (Holzer et al, 2013). The obtained data were statistically analyzed by the methods of descriptive statistics.

RESULTS

VEGF expression in the placenta was analyzed from the chorionic plate, villi to the basal plate of the placenta. In the amnion epithelium, the most of cells showed negative VEGF expression. Only a small part of

cells showed positive VEGF expression of very low intensity. VEGF expression in the amnion epithelium was evaluated as very weak, and the percentage of immunopositive cells was small 1+ (table 1, figures 1 and 2). In the stroma of the chorionic plate of the placenta, positive VEGF expression of medium intensity 2 was present in a small number of cells 1+ (table 1, figures 1 and 2). In the villous trophoblast, immunoreactivity for VEGF was very low and a small number of cells showed immunoreactivity for VEGF (table 1).

Table 1. The VEGF expression in normal term human placenta.

	VEGF expression in normal term placenta	
	Intensity of staining	Percentage of immunopositive cells
Amniotic epithelium	1	1+
Stroma of the chorionic plate	2	1+
Trophoblast	1	1+
Blood vessel endothelium	2	3+
Stroma of the villi	2	1+
Basal plate	2	1+

0 - negative, 1 - weak, 2 - moderate, and 3 - strong; 1+ = from 0 to 25% of cells were positive; 2+ = 25 - 49% of cells were positive; 3+ = 50 - 75% of cells were positive; and 4+ = >75% of cells were positive.

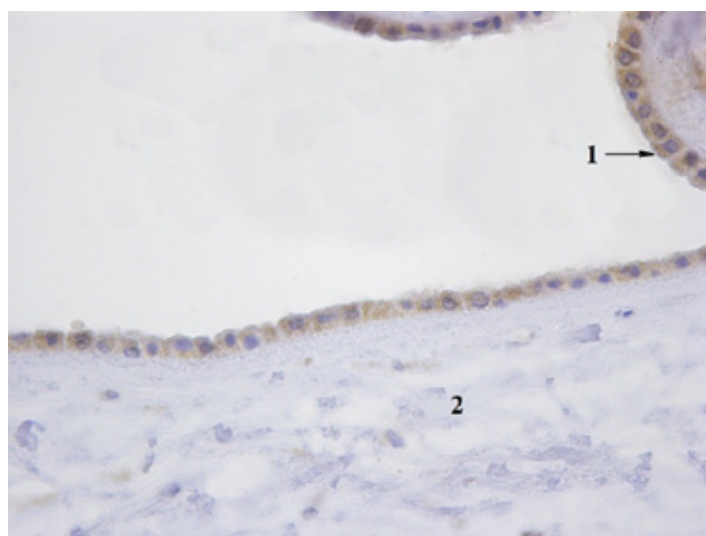


Figure 1. VEGF expression in the amniotic membrane: 1. positive VEGF expression in the amniotic epithelium, 2. amniotic membrane stroma (anti-VEGF 1:25, x 400).

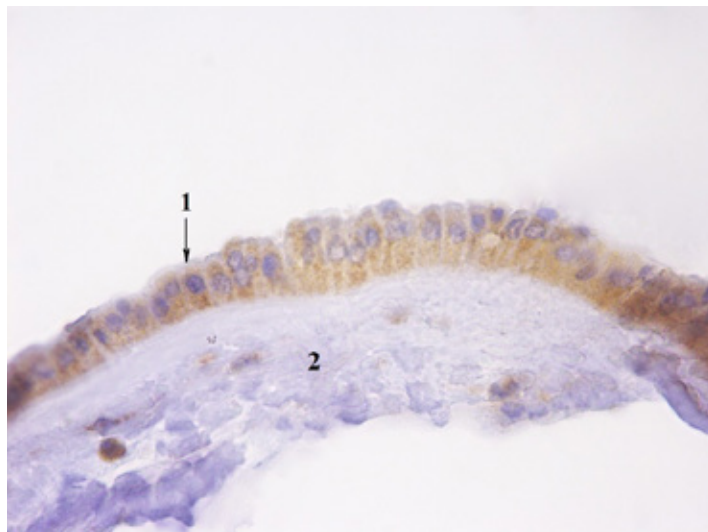


Figure 2. VEGF positive amniotic epithelium: 1. positive VEGF expression in the amniotic epithelium, 2. stroma of the amniotic membrane (anti-VEGF 1:25, x630).

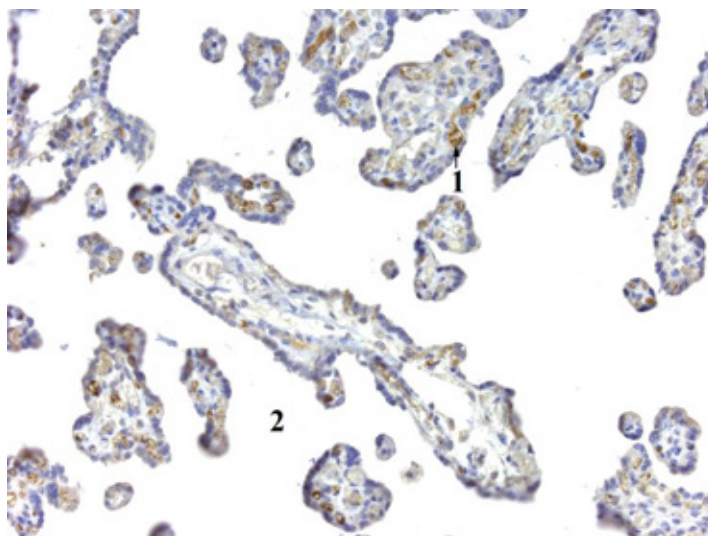


Figure 3. VEGF expression in the normal placenta: 1. positive VEGF expression in the endothelium of capillaries in the terminal villi, 2. intervillous space (anti-VEGF 1:50, x200).

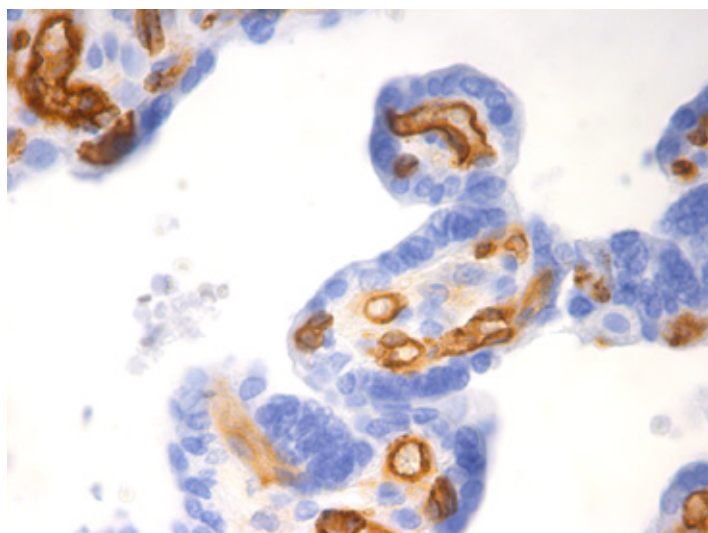


Figure 4. Positive VEGF expression in cells of the stroma of the villi and the endothelium of the villous capillaries (anti-VEGF 1:50, x630).

The most intense immunoreactivity for VEGF is present in the endothelium of the villi capillaries and larger blood vessels, arterioles, and arteries of the placenta (figure 3). Positive VEGF expression of moderate intensity was present in more than 50% of endothelial cells. VEGF expression in the endothelium was 3+ (table 1). Also, according to the number of blood vessels of the placenta that had positive VEGF expression, and with the limit of positivity which is more than 10% of all blood vessels, the VEGF expression in the blood vessels of the placenta was determined as positive. Immunoreactivity for VEGF was present in the stroma of the villi. Immunoreactivity of medium intensity – with category 2, was present in a smaller number of stromal cells of the villi – with category 1+ (table 1, figure 4).

In the basal plate, between the decidual cells, cells with a size smaller than the decidua cells and with positive VEGF expression in the cytoplasm were present. VEGF positive expression of basal decidua cells was of medium intensity - with category 2, and their number was category 1+ (table 1 and figure 5).

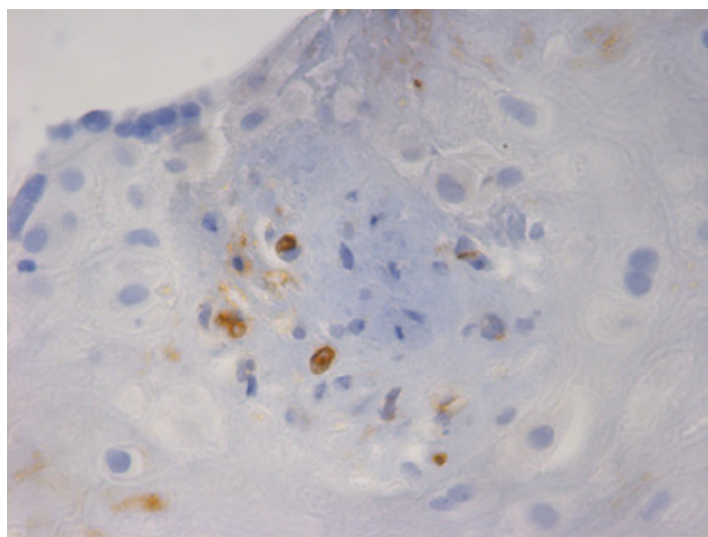


Figure 5. Positive VEGF expression in cells located between the decidual cells (anti-VEGF 1:50, x630).

DISCUSSION

Vascular endothelial growth factor, basic fibroblast growth factor, b-FGF, and endothelial nitric oxide are positive regulators of angiogenesis (Hendrix et al, 2019). They are strongly expressed during embryonic and fetal development, especially in the first trimester of pregnancy.

VEGF, also known as VEGF-A, is a protein that increases vascular permeability. It was originally obtained by purifying the liquid secreted by the tumor. Independently of the isolated protein from the fluid secreted by the tumor, a few years later, another protein with angiogenic activity was purified and isolated and named VEGF. Molecular cloning revealed that these two proteins are identical and they are encoded by a single gene.

The VEGF family of proteins includes VEGF-A, VEGF-B, VEGF-C, VEGF-D, placental growth factor (PlGF), and VEGF-E (Orf-VEGF). Except for the last member of the family, for the rest of these proteins of the VEGF family, there are five genes in the genomes of mammals, including humans.

In this study, positive VEGF expression was found in the amniotic epithelium, mesenchymal cells of the chorionic plate, trophoblast, stroma cells of the villi, endothelial cells of the placental blood vessels, and cells of the basal decidua. In the placenta, the most intensive immunoreactivity for VEGF was present in the endothelium of blood vessels. Immunoreactivity was medium to strong intensity, present in more than 50% of endothelial cells, with category 3+.

In the study by Schiessl and co-authors, VEGF expression was analyzed in the normal placenta through all three trimesters of pregnancy. Placental bed biopsies were obtained at 8–10, 12–14, 16–20, and 37–42 weeks of gestation (Schiessl et al, 2009). VEGF-A was localized in endovascular, intramural, and extravillous trophoblast at all examined gestational ages. There was no difference in the VEGF-A expression in the trophoblast across the gestational age groups.

Özgökçe and coworkers found in the normal placenta, between thirty and thirty-eight gestational weeks, moderate positive VEGF expression in the villi, blood vessel endothelial cells, syncytial cells, and Hofbauer cells (Özgökçe et al, 2022).

The study of Alahakoon and coworkers analyzed the immunolocalization of the angiogenic factor in different placental tissue types. VEGF was detected in syncytiotrophoblast, cytotrophoblast, extravillous trophoblast, endothelium, and Hofbauer cells (Alahakoon et al, 2018). Macrophages, decidua cells, and trophoblasts produce VEGF which is critical for the process of implantation (Wheeler et al, 2018).

Clark and coauthors showed with I-VEGF (VEGF labeled with sodium iodide) the major sites of action for VEGF, which were the endothelial cells within the fetal villi (Clark, 1998).

Invasive cytotrophoblast in early gestation has positive expression of VEGF-A, VEGF-C, placental growth factor, VEGFR-1, and VEGFR-3. At the time of delivery, the placenta has a positive expression for VEGF-A, PlGF, and VEGFR-1.

The trophoblast migrates in a retrograde direction along the wall of spiral arterioles (endovascular trophoblast), which it transforms into tubes of large diameter and low resistance. Endovascular trophoblast invasion occurs in a two waves. The first wave in the decidual segments of the spiral arterioles takes place from the 8th to the 10th week of gestation. The second wave of endovascular trophoblast invasion into segments of spiral arterioles in the myometrium takes place from the 16th to the 18th week of gestation. This physiological transformation is characterized by the gradual loss of the normal musculoelastic structure of the arterial wall and its replacement by an amorphous fibrinoid material in which trophoblast cells are embedded. These physiological changes are necessary for a successful pregnancy.

The roles of VEGF, b-FGF, and eNOS in placental angiogenesis may be altered in conditions such as IUGR. Placental angiogenesis, i.e. the regulation of vascular development, depends on complex relationships between these factors, which play an important role in the development of IUGR (Helske et al, 2001; Wu et al, 2023).

Positive expression of VEGF is present in villous and extravillous trophoblast. Evidence suggests that VEGF regulates trophoblast function by stimulating the release of nitric oxide.

In this study, the presence of cells with positive VEGF expression was found in the stroma of the villi and in the basal decidua. These VEGF positive cells may be macrophages. Research has shown the presence of macrophages called Hofbauer cells in the stroma of the villi, and the presence of macrophages of maternal origin in the decidua basalis. Recent studies have shown that macrophages synthesize VEGF.

At the point of contact between maternal tissue and fetal tissue, where fetal trophoblast cells enter the maternal decidua and remodel spiral arteries, decidual macrophages, and natural killer cells or NK cells are the largest and most significant population of immune cells (Thomas et al, 2021; Lash et al, 2022).

They promote angiogenesis and tissue remodeling. HBCs are also pro-angiogenic because they produce large amounts of VEGF and Sprouty proteins - Spry 1, 2, and 3 (Reyes et al, 2018). With the secretion of VEGF-A, osteopontin (OPN), MMP-9, and TIMP-1 they have a key role in the remodeling of blood vessels in the placenta (Lash et al, 2022). Also, they participate in the vasoregulation of placental blood vessels because they have the ability to produce prostaglandin E2 and thromboxane (Reyes et al, 2018). With the secretion of interleukins and chemokines, they participate in inflammation, and these factors also

have proangiogenic properties. In addition, HBC signal to placental fibroblasts via IL-6 and to villous cytotrophoblasts via osteopontin and GM-CSF (Thomas et al, 2021). HBCs secrete IL-1 β , IL-6, IL-8, IL-10, chemokines CCL2, CCL3 and CCL4, TGF- β , low levels of FGF-2. HBCs through interaction with endothelial cells, fibroblasts, and trophoblasts support the growth of the placenta and its homeostasis (Thomas et al, 2021; Lash et al, 2022; Reyes et al, 2018).

CONCLUSIONS

Positive VEGF expression is present in all parts of the normal term placenta. Positive VEGF expression of low intensity was present in a small number of cells of amniotic epithelium and trophoblast. Positive VEGF expression of moderate intensity was present in a small number of cells of the chorionic plate stroma, the stroma of the villi, and the basal plate. Positive VEGF expression of moderate intensity was present in more than 50% of endothelial cells of all placental blood vessels. Positive expression of VEGF in the cells of all parts of the placenta indicates a significant role of VEGF in the development of the placenta.

CONFLICT OF INTEREST

There are no conflicts of interest.

Financial support and sponsorship: None.

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Received: May 9, 2023

Accepted: June 23, 2023



DOI: 10.7251/QOL2303110S

UDC: 316.752:613.81/.84-053.6

Original scientific paper

LIFESTYLES AND RISK FACTORS FOR DEVELOPING NCDs AMONG STUDENTS OF HEALTH SCIENCES IN REPUBLIC OF SRPSKA

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ABSTRACT: Lifestyles develop throughout the life, but adolescence and early youth are important stages in acquiring healthy lifestyles habits. This is also vulnerable period for substance misuse, worsened diet habits and sedentary lifestyles linked to academic activities and responsible for developing non communicable diseases (NCD). Goal of the article is to analyse lifestyles habits and risk factors for developing NCD among students of health sciences. Study is conducted at the University Apeiron, Faculty of Health Sciences among students from first to fourth years of study. Specially designed questionnaire was prepared and distributed on line, anonymously and voluntarily fulfilled by students. Every fifth student is smokers, 5,1% consume alcohol daily, more males (12,1%) than females (2,9%) ($p<0,05$). Majority of males (42,2%) consumed alcohol drinks in one occasion during previous month, statistically more than females (21,2%) ($p<0,05$). More than two third of students eat fruits and vegetables daily and one third have regular meals. Moderate physical active are 42,3% of students, and physical inactive are more females than males ($p<0,05$). Risk factors for NCD have to be prevented with supportive policies in school environment and community. Students of health sciences should be a positive model of changing risk habits for NCD and saving future quality of life.

Keywords: lifestyles, risk factors, NCD, students, prevention of diseases.

INTRODUCTION

Lifestyle is a set of the multidimensional aspects of personal behaviour in daily activities such as consumption of different matters which are associated with life choice and impact of community (EULM, 2022). Daily behaviour of diet/nutrition, physical activity, substance use (consuming cigarettes, alcohol, drugs etc), social support and management of stress have an effect on life habits and perception of health. Healthy lifestyle habits have been continual shown to influence personal health and perception of three dimensions of health: mental, social and physical (Nyberg, 2022). All dimensions of health are in dynamic balance of daily habits and determination of social environmental. Socio-economic conditions, living standards, living with a family members and social interactions, occupation and education influence on daily life styles and have an impact on health (Soiminen M, 2022). Youth like to spend leisure time with friends in different physical activities and this kind of social support is very important to life styles of youth and healthy choice.

Young adults have the lowest risk of diseases but they are exposed to substance use with high risk of developing dependence and other problems during adult life. Young people are disproportionately affected than people in adult age but the risks accumulated and increased opportunity to non-communicable diseases (NCD) during life (WHO, 2023). Substance use are associated with mental health disorders and in young adults those risks are mainly undetected (WHO, 2023).

Each sixth adolescent in Euro World Health Organization (WHO) region is overweight and each fifth of them has no regular physical activity which is connected with NCD in older ages (WHO, 2021).

Physical inactivity and sedentary nature of many forms of work places and education increase urbanisation associated with risk of obesity and overweight in young adults (WHO, 2004).

Health of students in school environment is under social contribution of friends and teachers, educational programme and academic achievement which maintenance psychosocially, mentally and physically growth (Al-Shehri, 2002). Schools have capacity to learn student's good healthy choice and healthy lifestyles. According to "Health for All" Policy of World Health Organization and Education for All Policy of United Nations each community has commitment for supportive school environment which promote and improve health. Schools can serve a variety of ways to promote health, prevent diseases and injuries and reduce risks for diseases (WB, 1993). Today, the concept of school health goes beyond providing health education for students and creating environment for physical education and recreation including recommendation for healthy lifestyles according to WHO guidelines.

Students at the Faculty of Health Sciences have specific role in promoting healthy lifestyles because they are models of health behaviours which improve health but often social, school environment and community factors determine risk behaviours for developing NCD and have a negative effect on health (Short, 2015).

Social factors affect health behaviours of students through different parts of daily activities influenced by patterns of daily behaviour at home, among peer groups, in local community, media and advertising and exposed to smoking, alcohol consumption, sedentary lifestyles and unhealthy nutrition (Stephoe, 2010).

University is a period of responsibility in terms of lifestyle practices among young adults where students face stresses of achieving success in their academic goals living in conditions without awareness of risk adjustment to lifestyles and environment (Nasir, 2019). Healthy choices are individual responsibility in community in which every person has a role for promoting healthy lifestyle.

Goal of the article is to analyse lifestyles habits and risk factors for developing NCD among students of health sciences in Republic of Srpska, University Apeiron. Specific goal is to determine differences between socio-demographic and socio-economic characteristics among students with NCD risks.

MATERIAL AND METHOD

The research was conducted at the University of Apeiron, Faculty of Health Sciences in Banja Luka, during autumn 2022. All students have possibility to participate in the survey through information given by e-mail and university media about subject of survey and instructions to link with on line introduction of survey and anonymously fulfilling of questionnaire.

Sampling frame was consisted of students from different studies of health sciences: nurses, physiotherapists, sanitary engineering and laboratory. Only students who read instructions and voluntary fulfil questionnaire were sampled. Sample consisted of students from all fourth years of study.

For the purposes of this research a specially designed questionnaire was used to evaluate lifestyle-related attitudes and practices. General part of questionnaire consisted of basic socio-demographic characteristics of participants (gender, age, place of resident and educational background) and socio-economic conditions through determining their living condition status as a good, average and low.

Educational background is divided in general, medical and technical secondary school education but for reason for analysing students' behaviours, education is selected in health sciences and other sciences. Social support at home was measured by living with families and friends or living alone. Survey includes questions about work experience in health institution because this aspect shows broader view of participating students in community life and could influence students' behaviours.

Lifestyles habits are measured according to Eurostat 2018 guidelines and recommendations in Health interview survey (Eurostat, 2018). Daily smoking is consuming all types of cigarettes including

e-cigarettes and daily alcohol consumption is drinking a wine/beer more than 1 dcl, spirits more than 0,05 dcl and coloured flavoured drinks more than 2 dcl. For moderate physical activity we calculate fast walking, swimming or bicycle riding which takes 30-60 minutes. According to WHO recommendations regular meals are meals with 3 main dishes and 2 snacks, and daily consumption of fruits and vegetables is consuming one portion of these foods per day.

Risk factors are determined and measured according to the WHO STEP wise approach to noncommunicable disease risk factor surveillance (WHO; 2017).

In the statistical analysis were used descriptive measures and distribution of frequencies according to characteristics of participants presented in tables and graphs. Tests for measure statistical significance between characteristics were used prior to analyse parametric and non-parametric variables. To assess the significance of the difference between lifestyles of students and socio-demographic characteristics and socio-economic was used Hi square with the value of statistically significance $p < 0.05$. The statistical package for social sciences was used in data processing (SPSS for Windows, version 21.0, 2012).

RESULTS AND DISCUSSION

Students at the faculty of health sciences, those sampled were 137, among males are 24,1% and females 75,9%. Most of them are in group of young adults between 18-22 years (49,6%), living in urban places (88,3%) and with educational background of health sciences (67,9%) (Table 1). More than a half of respondents perceive their socio-economic status as a good (66,4%) and each eight of ten participants lives with a family or friends in primary social unit of community (Table 1).

More than a half of respondents (64,2%) have experienced working in health institutions and therefore it would be possible to be a role model for healthy lifestyles not only for peers, than prior for patients and other people in community.

Table 1. General characteristics of participants (N= 137)

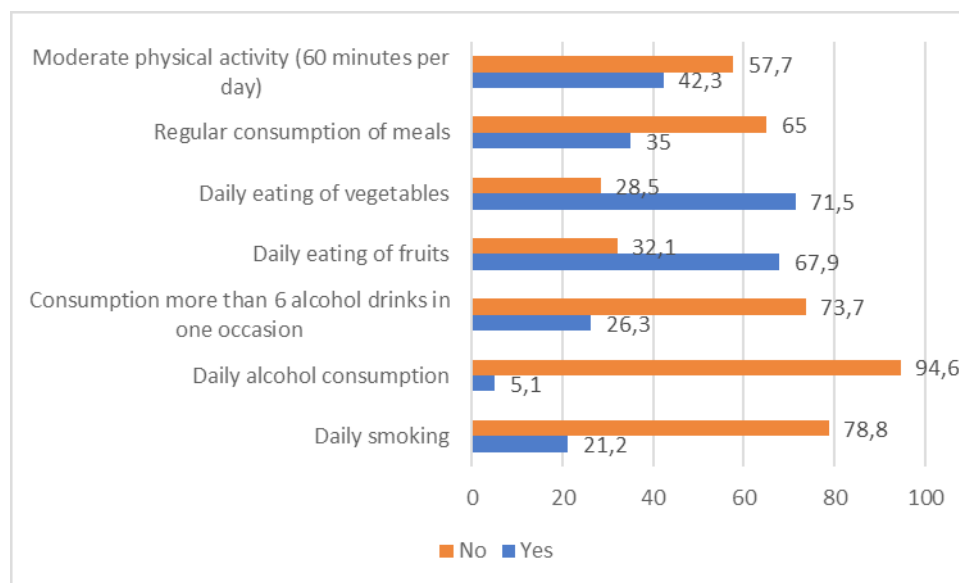
Sociodemographic characteristics	N	%
Gender		
Male	33	24,1
Female	104	75,9
Age groups		
18-22	68	49,6
23-27	40	29,2
8+	29	21,2
Place of resident		
Urban	121	88,3
Rural	16	11,7
Educational background		
Secondary school in health sciences	93	67,9
Secondary school in other sciences	44	32,1
Socio-economic status		
Good	91	66,4
Average	43	31,4
Low	3	2,2
Living with a family and friends		
Yes	113	82,5
No	24	17,5
Experience of working in health institution		
Yes	88	64,2
No	49	35,8

More than a fifth of students are daily smokers, less but not small percent of students are daily consumers of alcohol (5,1%) (wine/beer more than 1 dcl, spirits more than 0,05 dcl and coloured flavoured drinks more than 2 dcl) (Graph 1). Very important risk of youth lifestyle habits is consuming more than a six alcohol drinks in one occasion, and it is usual among 26,3% of students of health sciences. This indicator of youth health risks for developing NCD is measured value for all preventive activities which have to be done in school and university environment.

More than a third of students (35,0%) have regular meals, including 3 main and 2 additional, snack meals. More than a half of them eat fruits daily (67,9%) and more than a two third of them eat vegetables daily (71,5%) (Graph 1).

Moderate level of physical activity according to general recommendations of World Health Organization for young adults takes 30 minutes to one-hour of fast walking, swimming or bicycle riding which have 42,3% of students (Graph 1).

Graph 1. Percent of lifestyles habits among students



Risk factors for developing NCD are present in population of students. More than a fifth of females are smokers (24%), statistically significant more than males (12,1%) ($p < 0,05$). The greater number of smokers is among young adults older than 28 years (Table 2). Smokers are living mainly in urban areas, with good socio-economic status and general educational background (31,6%). Most of smokers are among students who don't have experience of working in health institutions (26,5%).

Daily consumption of alcohol is six time more among males (12,1%) than females (2,9%) ($p < 0,05$). Students with technical background consume alcohol daily more (8%) than others and they who are not living with family and friends (16,7%).

Less than daily use of fruits has more males (39,4%) than females (29,8%) (Table 2). Also, those habits have students who are living in urban places (34,7%) average socio-economic status (44,2%), and general educational background (47,4%) and those who don't have experience of working in health institutions (28,6%).

Less than daily use of vegetables has more males (33,3%) than females, youngers in 18-22 age groups (32,4%), general background (36,8%) living in urban areas (30,6%) and more than a third of those who don't have experience of working in health institutions.

Intakes of food not regularly have more females (68,3%) than males (54,3%), students with general background (73,7%) and those who have no experience of working in health institutions (73,9%) ($p<0,05$) (Table 2).

Physical inactivity is persistent among females (63,5%) more than males (39,4%) ($p<0,05$), students ages 28 and older (69%), are living in rural areas (75%), and in average socio-economic status (67,4%) ($p<0,05$) (Table 2).

Table 2. Sociodemographic and socioeconomic differences in lifestyles risks for developing NCD among students

Sociodemographic characteristics	Variable types	Daily smoking (%)	Daily alcohol consumption (%)	Consumption of more than 6 alcohol drinks in one occasion (%)	Less than daily use of fruits (%)	Less than daily use of vegetables (%)	Intake of foods not regularly (%)	Physical inactivity (%)
Gender	Male	12,1	12,1*	42,4*	39,4	33,3	54,5	39,4
	Female	24,0*	2,9	21,2	29,8	26,9	68,3	63,5*
Age group	18-22	14,7	4,4	33,8*	32,4	32,4	55,9	51,5
	23-27	25,0	7,5	30,0	27,5	27,5	72,5	60,0
	28+	31,0	3,4	4,3	37,9	20,7	75,9	69,0
Place of living	Urban	22,3	6,3	24,0	34,7	30,6	66,9	55,4
	Rural	12,5	5,0	43,8	12,5	12,5	50,0	75,0
Socio economic status	Good	22,0	6,6	29,7	26,4	25,3	60,4	54,9
	Average	18,6	2,3	20,9	44,2	32,6	74,4	67,4*
	Bad	33,3	0	0	33,3	66,7	66,7	0
Educational background	General	31,6	5,3	15,8	47,4	36,8	73,7	52,6
	Medical	18,3	4,3	26,9	31,2	26,9	66,7	55,9
	Technical	24,0	8,0	32,0	24,0	28,0	52,0	68,0
Living with family and friends	Yes	23,4	4,7	29,1	34,5	31,9	65,5	59,3
	No	16,7	16,7	16,7	20,8	12,5	62,5	50,0
Working experience in health institution	Yes	18,2	4,5	25,0	31,8	26,1	73,9*	59,1
	No	26,5	6,1	28,6	32,7	32,7	49,0	55,1

*- χ^2 ($p<0,05$)

In our study every fifth student smokes daily, less than in Poland study where every sixth student declared smoking, and more than 90% consumed alcohol (Jakubiec, 2015). In study provided among university students in Sarajevo (Brankovic, 2017) was the same percent of smokers like in our study. In Croatian study every third student smoked cigarettes every day (Malatestinić, 2015) and girls consumed more cigarettes than males, as well as in our study. In Croatian study, similar in our study, students consumed alcohol in one occasion, especially males but number of daily alcohol consumers is approximately 5% as well as in our study. Excessive alcohol drinking among males younger than 25 was in Americas study (US Department of Health and Human Services, 2015) which is associated with risk habits for NCD when youngers have experimental phases during occasions. British and Croatian authors describe the same situations between youngers male (Kuzman, 2004, Deetles, 2002). More than a third of students have regular meals which is similar to study provided in University of Sarajevo and more than in Poland study, where each ten students consumed regular meals. In study in Kuwait students have regular meals in more than two third of cases, and most of them consume daily fresh fruits and vegetables (Al-Sayeg, 2020). More than a two third of students in Banja Luka consumed fruits and vegetables daily while in German study 12,6% students consumed fruits and vegetables daily. (Tobish, 2015).

Moderate physical activity has under half of students in our study which is less than in Sarajevo University, but in Poland study most respondents preferred passive forms of recreation, only one in three practiced sports in their spare time. Moderate physical activity have about half of students in German and Kuwait study.

Compare lifestyles between students' population in different countries of Europe and broader there are no big differences with significantly increased of risk for developing NCD among females more than males.

CONCLUSIONS

Lifestyles of students of Health Sciences at Apeiron University in Banja Luka are positive habits for healthy choices in more than two thirds of them who eat fruits and vegetables daily, half of them who have moderate physical activity and more than third of them who have regular meals. Risks for developing NCDs are persisted among more than fifth of them who are daily smokers and consumers more than six alcohol drinks in one occasion. Changes in those habits have to be the result of environmental and societal changes associated with supportive policies in sectors such as health, agriculture, urban planning, marketing and education. According to WHO Health in All policies all of us in different sectors must be educators for young people, who live and work with us in family and community.

Promoting healthy lifestyles among students will save future families, communities and countries.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Recived: May 29, 2023

Accepted: June 23, 2023



DOI: 10.7251/QOL2303117S

UDC: 613.81/.84-053.6:316.752(497.6)

Original scientific paper

SELF-RATED HEALTH AMONG STUDENTS OF HEALTH SCIENCES IN BOSNIA AND HERZEGOVINA

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ABSTRACT: Self-rated health is associated with health behaviour and socio-demographic and socio-economic conditions on the way that health risks and poor socio-economic status determine poor self-rated health. The aim of the study was to determine self-rated health among students, perceive health behaviour risk and association with socio-demographic and socio-economic characteristics of students.

Methods: Study is conducted as a cross-sectional study among students of health sciences in autumn semester 2022. Year. Specially designed questionnaire was constructed based on international guidelines. Anonymously filling out an on line formed questionnaire by voluntary signing on university web site.

Results: More than three quarter of students perceived their health as a good and no one perceived health as a poor. Most students perceived their health as good (83,2%), mainly students with a technical background and those who are living in good socio-economic conditions (89,0%) ($p < 0,05$). The most frequent health risks among students are lack of physical activity (44,5%) and less than six hours for sleep and rest (43,8%). More than a third of students perceived fear, nervousness and tension (34,3%), a lack of time for friendship and family (33,6%) and irregular diet (31,4%). Every seventh student perceived overweight and obesity. Students who are living in poor socio-economic conditions perceived more health risks as well as those who don't have medical background and who are employed. More students in urban area perceived mental problems than those in rural areas.

Conclusion: Students are mainly perceived their health as a good and have health risks which will be reduced through health promotion in university educational programmes.

Keywords: perception of health, self-rated health status, risk behaviours, students.

INTRODUCTION

Perception of health is a measure for health status and all its components: mental, physical and social health rated on good, average and poor level of health status (WHO, 1952; Bailis, 2003). Self-perception is a statement about one's observation and definition of oneself health status, health behaviour and capability to functioning in social environment (Robak, 2005). This measure of health has been used extensively in epidemiological studies to determine population's state of health based on self-rated observation and explanation and due to its easy accessibility in population surveys has been used to establish differences in health status and risks for health between populational groups (Gold, 1996). The self-rated health is a reliable and valid measure of health and well-being for adolescent health research (Waters, 2001). The significantly lower scores reported by adolescents are associated with risk health behaviors, stress and illness.

Risk health behaviors such as unhealthy habits are often psychosocial reaction to factors from social environment and social support represent key elements for good health (Marmot, 2001). Study findings explore association between measures of socio-economic status and socio-economic conditions such as experiences of lack of social support with health behavior and self-rated or perceived health status.

Poor self-rated health was most common among persons who lacked social support, or who had poor socio-economic conditions (Kawachi, 1999; Molarius, 2006). Individuals with low values of self-perceived health have problems in functioning in social environment and very often have low socio-economic status measured in income, education and social and health care resources in community (Miilunpalo, 1997).

Studies have also found that sedentary lifestyle as well as overweight or underweight is more often associated with risks for health, such as tension, sleeplessness and other mental problems (Molarius, 2006). Lack of physical activity is associated with poor self-perception of health status as well as poor diet habits (Nowak, 2006; Vingilis, 2002). Overweight and obese people are more likely to report poor self-rated health in comparison to those with normal body mass index (Dubikaytis, 2014). Those common risk factors determine lower level of self-rated health status and increase risk of chronic non-communicable diseases. (Wichowski, 2008).

Health promotion behaviors are necessary for young people because they improve health perception which in turn enable the maintenance of physical, mental, and social well-being (Kim Y, 2018). In school environment there is need to implement educational program which improves skills for healthy choices and health behavior which protect health and reduce risks for diseases.

Students at the Faculty of Health Sciences have the right to educate and create social environment which is supportive of a healthy lifestyle and offer possibilities to reduce risks for health and promote healthy choices (Tafireyi CGS, Grace JM., 2022).

The aim of the article is to define the self-perceived level of health status and health behavior risks among students of faculty of health sciences and association with socio-demographic and socio-economic conditions in community.

MATERIAL AND METHOD

The study was conducted among students of the Faculty of Health Sciences in the Republic of Srpska, Bosnia and Herzegovina in autumn semester of 2022. year. In the sampling procedure, all students from different study programmes were selected: nurses, physiotherapists, sanitary engineering and laboratory engineering. Information about survey purpose and voluntary participation was given by e-mail and university media. Students who voluntarily participated are completed on line form of questionnaire, which is posted at the web site of the Faculty of Health Sciences.

For the purposes of this research a specially designed questionnaire was used to evaluate self-rated of health status and differences between socio-demographic characteristics of participants (gender, age, place of resident and educational background) and socio-economic conditions selected in three categories: good, average and poor according to European Union Survey on Income and Living Conditions (EU-SILCHO) (OECD, 2022).

Self-rated health status is based on perception of own health behaviour and classified as good, average and poor health based on answer: "How do you rate your general state of health?"

Educational background that previously had students in former secondary school is classified as general, medical and technical education. Work experience in health institutions shows professional activity of students during study and social support at home defined by living with families and friends or living alone.

Self-perception about health behaviour describe perception of diet and nutritional habits, usually mental health symptoms, daily physical activity, leisure time for friendships and family and less than minimum time for sleep and rest (six hours) as a risk for mental and physical health. Perception about own health risks is measured according to Eurostat recommendations for Health interview survey (Eurostat, 2018), based on questions "How do you assess, do you have some of the following risks factors for health?" Clarifications about statements are listed in text of questions.

The World Health Organization (WHO) defined obesity as those people with the body mass index (BMI) of equal or greater than 30, and overweight as those whose BMI are between 25.0 and 29.9. (WHO; 1995).

For the statistical analysis are used descriptive measures and distribution of frequencies according to level of perceived health status and characteristics of participants. To compare the frequency of the given categories of quantitative characteristics in the analysed groups the Hi square test is implemented. A significance level was established at $p=0.05$ for the values included in the critical region of a given distribution. All p values were two sided and $p < 0.05$ was set as statistically significant. The statistical analyses were made with the use of SPSS for Windows, version 21.0, 2012.

RESULTS AND DISCUSSION

Females are represented three times more (75,9%) than males (24,1%) in a sample of 137 students. Most of them perceived own health status as a good (83,2%), and no one perceived health as a poor. Among them, the largest number of students who perceived good health are in age group 23-27 years (87,5%) (Table 1).

Good socio-economic conditions are significant (89,0%) associated with good self-perception of health status and poor social conditions are significant associated with average rated health status (33,3%) ($p < 0,05$). Students who finished technical secondary school perceived their health as a good (92,0%) more significant than students from technical and general secondary schools ($p < 0,05$). Financial support from family determines good self-perceived health as well as living in rural areas (Table 1).

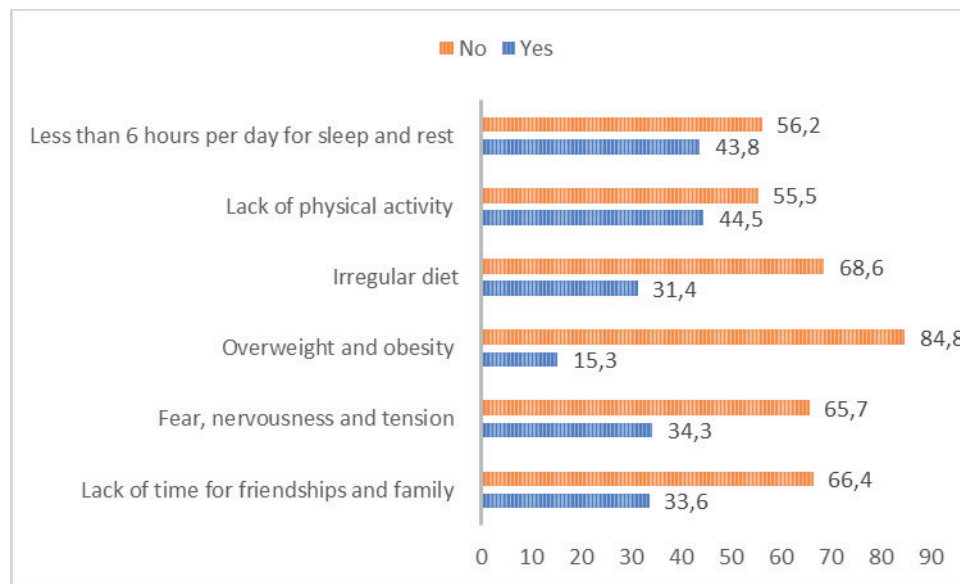
Table 1. Sociodemographic and socioeconomic differences in self-rated health status among students in Banja Luka

Sociodemographic characteristics of participants	Variable types	Students in sample		Self-rated of health status			
				Good		Average	
		Number	%	Number	%	Number	%
All	Total	137	100	114	83,2	23	16,8
Gender	Male	33	24,1	29	87,9	4	12,1
	Female	104	75,9	85	81,7	19	18,3
Age group	18-22	68	49,6	56	82,4	12	17,6
	23-27	40	29,2	35	87,5	5	12,5
	28+	29	21,2	23	79,3	6	20,7
Place of living	Urban	121	88,3	99	81,8	22	18,2
	Rural	16	11,7	15	93,8	1	6,3
Socio economic status	Good	91	66,4	81	89,0*	10	11,0
	Average	43	31,4	31	72,1	12	27,9
	Poor	3	2,2	2	66,7	1	33,3*
Educational background	General	19	13,9	11	57,9	8	42,1
	Medical	93	67,9	80	86,0	13	14,0
	Technical	25	18,2	23	92,0*	2	8,0
Living with family and friends	Yes	113	82,5	94	83,2	19	16,8
	No	24	17,5	20	83,3	4	16,7
Financial support during study	Family	54	39,4	46	85,2	8	14,8
	Employed	83	60,6	68	81,9	15	18,1
Working experience in health institution	Yes	88	64,2	72	81,8	16	18,2
	No	49	35,8	42	85,7	7	14,3

*- χ^2 ($p < 0,05$)

Self-perceived health behavioral risks among students are lack of physical activity which have 44,5% of students, and 43,8% have less than 6 hours per day for sleep and rest (Graph 1).

More than third of them perceived irregular diet and fear, nervousness and tension and insufficient time for friendships and family. Every seventh student perceived own body mass index overweight or obesity (Graph 1).



Graph 1. Percent of self- perceived health risks among students

Self-perception of risk factors are determined by students and their opinion about own behavior which reflects on health. More males (18,2%) than females (14,4%) perceived that they are overweight or obese, most of them in age group 23-27 years (22,5%) (Table 2). Students who finished secondary medical school perceived this risk (17,2%), also, those who are living in urban area (15,7%) and in average socio-economic status (23,3%).

Irregular diet as a risk factor perceived more females (34,6%) than males (21,2%), and all students live in average socio-economic status ($p < 0,05$), students with medical background perceived this risk in most cases (36,6%), as well as those who have experience working in health institutions (37,5%) ($p < 0,05$) (Table 2).

Lack of physical activity perceived more females (49,0%) ($p < 0,05$), who are living in average socio-economic conditions (48,8%), rural areas (50,0%) and with technical background in secondary school (52,0%) (Table 2).

Lack of time for friendships and family have more males (36,4%), and young adults older than 28 years (48,3%) (Table 2). Students who are employed (47,0%) perceived their socio-economic conditions as an average (51,2%) and have experience of working in health institutions (42,0%). They don't have enough time for friendships and family ($p < 0,05$).

Less than six hours per day for sleep and rest have more females (45,2%), those who are living in urban areas (45,5%), in poor socio-economic conditions, and statistically significant more students who have finished general secondary school (57,9%), and who are employed (53,0%).

Sense of fear, nervousness and tension perceived more by females (37,5%) than males (24,2%), those who are living in urban areas (37,2%) ($p < 0,05$), in poor socio-economic conditions (66,7%), with general background in secondary school (57,9%) and who don't have experience working in health institutions (44,9%) ($p < 0,05$) (Table 2).

Table 2. Sociodemographic and socioeconomic differences in self-perception of health risks among students in Banja Luka

Sociodemographic characteristics	Variable types	Lack of time for friendships and family (%)	Fear, nervousness and tension (%)	Overweight and obesity (%)	Irregular diet (%)	Lack of physical activity (%)	Less than 6 hours per day for sleep and rest (%)
Gender	Male	36,4	24,2	18,2	21,2	30,3	39,4
	Female	32,7	37,5	14,4	34,6	49,0*	45,2
Age group	18-22	29,4	36,8	10,3	29,4	38,2	42,6
	23-27	30,0	27,5	22,5	30,0	47,5	50,0
	28+	48,3	37,9	17,2	37,9	55,2	37,9
Place of living	Urban	34,7	37,2*	15,7	33,9	43,8	45,5
	Rural	25,0	12,5	12,5	12,5	50,0	31,3
Socio economic status	Good	25,3	38,5	11,0	26,9	42,9	40,7
	Average	51,2*	23,3	23,3	100*	48,8	46,5
	Poor	33,3	66,7	33,3	32,6	33,3	100
Educational background	General	21,2	57,9	15,8	21,1	47,7	57,9*
	Medical	37,6	29,0	17,2	36,6	41,9	47,3
	Technical	28,0	36,0	8,0	20,0	52,0	20,0
Living with family and friends	Yes	35,4	33,6	16,8	33,6	45,1	46,0
	No	25,0	37,5	18,3	20,8	41,7	33,3
Financial support during study	Family	13,0	42,6	16,7	27,8	44,4	29,6
	Employed	47,0*	28,9	14,5	33,7	44,6	53,0*
Working experience in health institution	Yes	42,0*	28,4	13,6	37,5*	44,3	47,7
	No	18,4	44,9*	18,4	20,4	44,9	36,7

*- χ^2 ($p < 0,05$)

Our findings suggest that self-rated health is not only a spontaneous assessment of one's health status and related practices than many socio-demographic and socio-economic factors are significant associated with own perception s'of health.

Self evaluation of health state is more often good, or moderate among young adults. No one perceived their health as a poor which correlates with other authors (Schwarzwald, 2005, Erginoz, 2004). In our study males perceived their health as a good (87,9%) more often than females (81,7%) but in Brazil study females perceived their health (48,2%) more often than males (46,9%) (Schwarzwald, 2005).

Moreover, the effects of several factors from social environment reflect on respondents' self-rated health, varied according to whether respondents perceived their health risks in own behaviour. Effects of risk factors and health behavior are mediated by more specific health problems and their functional consequences (Manderbacka, 1999). According to survey data higher level of education, higher income, being male and have social support were found to be associated with high level of self-perception of health status (Piko, 2000, 2007). According to our study, results are very similar, those who live in better social conditions, with family and friends support, being male and with medical secondary background perceived their health as a good.

However, educational background impacts on health behaviors and self-rated health. Students who previously had secondary medical school perceived their health in most cases as a good (86,0%). Also, socio-economic status determine health as a good in most cases (89,0%) of a good perceived socio-economic status which is similar in Turkish study (Erginoz, 2004). Most of students have lack of physical activity (44,5%), as well as less than six hours per day for sleep and rest (43,8%) which perceived more females than males, students who are living in average socio-economic status and students who are employed. Our

study results are very similar study in Mexico (Nayheli, Villegas, Deygadillo, 2022). Lack of physical activity is often associated with perception of overweight and obesity by students and other mental problems like anxiety (Kirkcaldy, 2002). Overweight and obesity among each seventh young respondents were found to have an health risks in our study, while in study in Iran perceived the same health problems one of five students (Mann, 2016). This may reflect the effects of health problems not captured by our indicators of ill health, but may also indicate that risk factors and risky behaviours are considered to have an effect on one's perceived health even in the absence of health consequences. Results of our study reflect that more than third of students have irregular diet and perceived health risks through fear, nervousness and tension and inadequate time for freindships and family which is very similar in other studies (Luppino, 2010; Hudd, 2000; Nayheli, Villegas, Deygadillo, 2022).

It is known that demographic factors like age, residence type, education and school background have great role in determining health behaviors (Larouche, 1998). Most of health risks perceived by students in our study are dominated among young adults older than 28 years, living in urban areas, and average and poorer perceived socio-economic status. Females perceived health risks in mental problems, insufficient sleep and rest, lack of physical activity and irregular diet more than males while males pereived inadequate time for friendships and family and being overweight and obese more than women.

CONCLUSIONS

Students who finished technical secondary school and live in good socio-economic conditions (89,0%) significant perceived their health as a good ($p < 0,05$). Two quarter of students have lack of physical activity and less than six hours of sleep and rest a day. More than third of students have fear, inadequate and irregular diet. Females significantly perceived risk of lack of physical activity (49,0%) than males (30,3%) ($p < 0,05$). Males perceived more than females lack of time for friendship and family (36,4%) and students who live in average socio-economic conditions (51,2%) and employed (47,0%) ($p < 0,05$). Fear, nervousness and tension have students who live in urban area (37,3%) more than in rural ($p < 0,05$). Irregular diet perceived more students who have experience working in health institution (37,5%) and those who live in average socio-economic conditions ($p < 0,05$).

According to this study, a big number of health sciences students are not adopting health promoting lifestyle behaviors on daily basis and their life-style behaviors are at risk. Therefore, researchers would like to recommend that university could facilitate student learning about health and link this living a healthy lifestyle.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Received: May 29, 2023

Accepted: June 29, 2023



DOI: 10.7251/QOL2303124D

UDC: 616.379-008.64-06:617.586

Original scientific paper

OBESITY AS A RISK FACTOR FOR DIABETIC FOOT ULCER

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ABSTRACT: Introduction: Diabetic foot is a term used to describe the foot of a diabetic patient with a potential risk for several pathological consequences, including infection, ulceration and/or destruction of deep tissues associated with neurological abnormalities and different degrees of peripheral vascular disease and/or metabolic complications of diabetes in lower extremities. **Objective:** To determine the relationship between body mass index (BMI) and the characteristics of diabetic foot ulcer, and to offer an answer to the question of whether and in what context obesity can be viewed as a risk factor for diabetic foot ulcer or as a predictor of treatment outcomes. **Methods:** The study was created as a prospective follow-up study, and the total sample contained 33 subjects. Subjects were adult patients of both sex that satisfied determined inclusion criteria. The consent of the competent ethics committee was also obtained. All data were entered into the MS Excel database, and further statistical processing was performed using SPSS 21 program. Statistically significant difference was noted if $P \leq 0.05$. **Results:** The key results of this study are the fact that no statistically significant correlation was found between the diameter and depth of the ulcer at first examination with BMI values ($P = 0.865$ and $P = 0.137$), as well as obesity expressed through BMI with the clinical outcome of diabetic foot ulcer treatment after 2 months ($P = 0.448$). **Conclusion:** There is no proven statistical relationship between diameter and depth of ulcers with BMI, nor the influence of BMI on the clinical outcome of diabetic foot ulcer treatment.

Keywords: diabetic foot ulcer, body mass index, obesity, diabetic polyneuropathy, amputation.

INTRODUCTION

Diabetic foot, according to the World Health Organization (*WHO*), is the term for the foot of a patient suffering from diabetes, with the potential risk of a number of pathological consequences, including infections, ulceration and/or destruction of deep tissues associated with neurological abnormalities, various degrees of peripheral vascular disease and/or metabolic complications of diabetes in the lower extremities (Novinščak, 2010). The mechanism of diabetic foot formation is multifactorial and complex. A sedentary lifestyle in combination with the accumulation of excess weight triggers the pathophysiological processes of increased body resistance to insulin, which is the basis of the development of type 2 diabetes (Boulton, 2002). Broadly speaking, the two main causes of diabetic foot ulcers are peripheral neuropathy and ischemia. Percentagewise, 60% are neuropathic ulcerations, 20% are ischemic, and 20% are mixed ulcerations (Amstrong, Boulton & Bus, 2017). Male gender, duration of diabetes, smoking, poor foot hygiene, wearing inadequate footwear, poor glycoregulation, presence of eye, cardiovascular and renal complications were also identified as risk factors for the development of diabetic foot. Obesity is also one of the factors that can contribute to increased load on the anatomical structures of the foot (primarily blood

vessels and muscles) (Reardon & Simring, 2020). There are projections that by 2030, 6% of the world's population will suffer from diabetes, and that every fourth patient will develop a diabetic foot, while 10 to 30% of these patients will have an amputation (Huljev & Gajić, 2013). Also, there are data that about 25% of people who are treated for diabetes develop diabetic foot, and up to 15% experience amputation. That's why early detection of people with a tendency to develop diabetic foot is a basic condition for adequate treatment, which reduces the risk of amputation. Diabetic foot treatment takes a long time, costs a lot, and the results are often unsuccessful (Metelko & Brkljačić Crkvenčić, 2013). The key to successful treatment of chronic wounds is based on correct diagnosis and modern recognition and discovery of the cause of their occurrence; optimal care conditions; treatment of local and systemic infection; control of local and systemic disorders in the body and prevention of further trauma, as well as correction of hypoxia and stimulation of host tissues to cause an adequate healing process (Situm & Kolić, 2011). Treatment of patients with diabetic feet involves a multidisciplinary approach by a team of experts. There are a number of treatment modalities that include surgical debridement, regular dressings, targeted application of antibiotics according to the results of the antibiogram and treatment of the underlying diseases, as well as other local and supplementary measures. If treatment is not achieved, surgical treatment (amputation) is an option (Driver et al, 2010). In the medical literature, there is very little data on the relationship between diabetic ulcers and body mass index, or data on the relationship between the healing speed of diabetic foot ulcers and body mass index, which was the main reason for creating such a study.

RESEARCH OBJECTIVES

To determine the relationship between body mass index (BMI) and the characteristics of diabetic foot ulcers in patients who are currently treated with hyperbaric oxygenation as an additional therapeutic modality.

To offer an answer to the question of whether and in what context obesity can be considered a risk factor for the occurrence of diabetic foot ulcers or as a predictor of the outcome and length of treatment for diabetic foot ulcers.

MATERIAL, SUBJECTS AND METHODS

The research was designed as a prospective follow-up study. The total sample contained 33 respondents and was collected in the time period from November 1, 2021. until April 1, 2022. The subjects were adult patients of both sexes who were treated or are being treated at the Center for Hyperbaric Medicine and Chronic Wound Treatment, Institute for Physical Medicine and Rehabilitation "Dr. Miroslav Zotović" Banja Luka, for the treatment of diabetic foot ulcers. Inclusion criteria were: indicated treatment for diabetic foot ulcer and patient's signed consent to participate in the study. Exclusion criteria were: no confirmed diagnosis of diabetic foot ulcer; the consent form for participation in the study was not signed, or the patient subsequently withdrew from participation.

The device-type study tools used during the research are a centimeter altimeter, a calibrated scale, a centimeter tape, and a camera. Other materials, drugs, equipment, and medical devices used are part of the standard work process and are in the domain of medical treatment of diabetic foot ulcers. The questionnaire on the first day (diabetic foot ulcer follow-up start) contained questions related to: general data with general anthropometric and demographic data and measurements of the patient and data on the diabetic foot ulcer). This part also contained data on measurements entered by the main researcher. The second part of the questionnaire (at the end of diabetic foot ulcer follow-up – after 2 months) contained data on the outcome of treatment and the appearance of the diabetic foot ulcer (this data was also entered by the researcher). With

the consent of the patients, the Informed Consent was signed and a photo gallery of diabetic foot ulcers was created at the start of treatment (1st day) and at the end of treatment (i.e. after 2 months). It is important to emphasize that these were standard procedures and measurements and that no adverse events were expected. The consent of the Management of the Institute for Physical Medicine and Rehabilitation “Dr. Miroslav Zotović” Banja Luka and the consent of the Ethics Committee of the Institute for Physical Medicine and Rehabilitation “Dr. Miroslav Zotović” were obtained. All the collected data were entered into the MS Excel database, and further descriptive processing was carried out with a graphic presentation of the obtained data, as well as the calculation of statistical inference tests using the SPSS 21 program. The assessment of data distribution was performed with the help of the *One-Sample Kolmogorov-Smirnov Test*, and for data which distribution is not normal, non-parametric tests (*Mann Whitney U Test*, *Kruskal Wallis Test*) were performed, while for data where the distribution is normal, parametric tests were performed (*Studentov T Test*, *ANOVA Test*). *Chi Square Test* was used to compare categorical data. As statistically significant values are taken those where $P \leq 0.05$.

RESULTS

The study included 33 respondents, average age 62.9 ± 9.9 years, of which 75.8% were men. The mean age of the subjects was 62.9 ± 9.9 years; average height 177.5 ± 7.8 cm; mean BMI 26.8 ± 4.2 kg/m², with average duration of diabetes 11.1 ± 6.6 years (Tables 1 and 2).

Table 1. shows the frequencies and percentages of the observed variables (gender, age groups and BMI categories and clinical outcomes). Results are presented as frequency and percentage.

DATA	N (%)
♂ gender	25 (75.8%)
♀ gender	8 (24.2%)
40-49 years	5 (15.2%)
50-59 years	8 (24.2%)
60-69 years	11 (33.3%)
≥ 70 years	9 (27.3%)
BMI 18.5-24.9 kg/m ²	8 (24.2%)
BMI 25-29.9 kg/m ²	20 (60.6%)
BMI 30-34.9 kg/m ²	4 (12.2%)
BMI ≥35 kg/m ²	1 (3%)
Complete healing of the ulcer	10 (30.3%)
Ulcer reduction	12 (36.4%)
Inpatient finding of ulcer	7 (21.2%)
Worsening of ulcers	0 (0%)
Limb amputation	4 (12.1%)

Table 1. Frequencies and percentages for parameters: gender, age groups, BMI categories and clinical outcome

Table 2. presents the mean values and standard deviation of the observed parameters/median with IQR, depending on whether the data distribution is normal.

DATA	X ± SD	Mediana (IQR)
Age (years)	62.9 ± 9.9	-
Body mass (kg)	-	81 (76-90)
Body height (cm)	177.5 ± 7.8	-

Body mass index (kg/m ²)	26.8 ± 4.2	-
Duration of diabetes (years)	11.1 ± 6.6	-
Ulcer diameter - 1st examination (cm)	-	1.5 (1.0-1.5)
Ulcer depth - 1st examination (cm)	-	0.5 (0.0-0.5)

Table 2. Mean values and standard deviation of observed parameters/median with IQR - depending on the type of distribution.

Table 3. shows statistical testing of the influence of obesity expressed through BMI on ulcer diameter and ulcer depth.

	BMI 18.5-24.9	BMI 25-29.9	BMI 30-34.9	BMI 35-39.9	BMI ≥ 40	P value
DIAMETER OF ULCER	1.50	1.50	1.25	-	1.50	
Median (IQR)	(1-1.25)	(1-2)	(1-1.50)		(1.50-1.50)	0.865**
ULCER DEPTH	0.35	0.35	0.5	-	1	
Median (IQR)	(0.05-0.87)	(0-0.5)	(0.35-0.87)		(1-1)	0.137**

* One way ANOVA

**Kruskal Wallis test

Table 3. Statistical testing of the influence of obesity expressed through BMI on ulcer diameter and ulcer depth.

Table 4. shows statistical testing of the influence of age, duration of diabetes and BMI on the clinical outcome of diabetic foot ulcer treatment after 2 months.

	In total	Healing	Reduction	Stationary	Worse	Amputation	P
AGE (X ± Sd)	62.94 ± 9.90	59.2 ± 9.10	63.33 ± 9.33	64 ± 12.14	0	72.25 ± 4.11	0.164*
DURATION OF DIABETES Median (IQR)	10 (6.50- 15.00)	7.50 (5.75-12.25)	11 (7.25-19.50)	12 (6-24)	-	9 (4.25-13.75)	0.491**
BMI Median (IQR)	26.60 (24.60- 28.35)	26.05 (23.95- 28.17)	27 (26.32- 30.35)	26.80 (21.50- 27.70)	-	27.60 (21.90- 31.42)	0.448**

* One way ANOVA

**Kruskal Wallis test

Table 4. Statistical testing of the influence of age, duration of diabetes and BMI on the clinical outcome of diabetic foot ulcer treatment after 2 months

DISCUSSION

Some literature extracts also speak in favor of a higher representation of the male sex, as is the case in this study (75.8%) (Table 1), while hormonal differences and an increased tendency to develop neuropathies and vascular diseases in people are often cited as possible reasons for male gender (Coleman et al, 2013). When it comes to age distribution, in one of the literature excerpts it is found that the largest proportion of subjects with diabetic foot ulcers were aged 58-67 years, 22.6%, while when it comes to BMI, there was 29.6% in the obese category (Bekele et al, 2019). However, we are talking about a study that was carried out in Ethiopia, so these results cannot be completely compared with the results of this research (from Table 1), considering the different climate, race, habits, environmental factors, and others. When it comes to the clinical outcome of treatment after 2 months, in 30.3% of patients the ulcer was completely

healed, in 36.4% the ulcer decreased, in 21.2% the ulcer had a stationary finding. No deterioration in diameter was recorded, while 12.1% of subjects had to undergo amputation during the two-month period of treatment and observation (Table 1). Amputation of the lower extremities is most often closely related to a diabetic foot ulcer, which is usually preceded by the development of an infection. In the literature, it is found that in people who have an active diabetic foot ulcer, the final recovery process is 65-75% (Vadivello et al, 2018). Information on the amputation rate of 30.43% was also found, however, the time of follow-up of the patients is not stated, and this information should be taken with reservation in relation to the result of 12.1% of amputated patients in this study (it is possible that some ulcers that are marked as inpatients require amputation) (Bekele et al, 2019). Very important facts when analyzing the percentage of amputee patients is the availability of quality health care for such patients. The high rate of amputations in diabetic foot ulcer patients does not necessarily mean severe forms of the ulcer, but it is sometimes a reflection of poor care and a “laxer” attitude to the decision on surgical treatment that includes amputation.

As a key finding in this research, we single out the fact that no statistically significant correlation was found between ulcer diameter at the first examination and BMI values (observed through defined BMI categories) ($P=0.865$). In this calculation, we took into account the distribution of the median and IQR values of the ulcer diameter in each defined BMI category. We also did not find a statistically significant association between ulcer depth at the first examination and BMI values (observed through defined BMI categories) ($P=0.137$). However, a detailed analysis shows that a greater depth of the ulcer corresponds to a higher BMI, so in patients with a $BMI \geq 40$, the median ulcer depth was 1 cm, while for BMI 18.5-24.9 the median was 0.35 cm, for BMI 25-29.9 and 30-34.9 the median was 0.5 cm (Table 3). Although the statistical significance of this difference was not proven, these values indicate that patients with a higher BMI have a greater depth of ulcer changes. So, as an answer to the first question of the hypothesis, we can say that the depth of the ulcer increases with the increase in BMI, while the diameter of the ulcer has no statistical association with BMI values.

In this study, we also found no statistically significant association of obesity expressed through BMI with the clinical outcome of diabetic foot ulcer treatment after 2 months ($P=0.448$), as well as with age and duration of diabetes (Table 4). In this calculation, we took into account the distribution of the median and IQR values for BMI according to the defined possible categories of clinical outcome (complete healing, reduction of ulcer, stationary finding, worsening of ulcer, and amputation of external limb). So, as an answer to the second question from the hypothesis, it can be said that we did not find a correlation between BMI and the outcome of diabetic foot ulcer treatment. One possible reason is the small sample size.

In general, the prevalence of overweight has increased dramatically in the USA over the past 50 years, so we find that in 2010, 69.2% of the population had a BMI greater than 25. Furthermore, it is believed that in the next 20 years in the USA, obesity will continue to grow, and that in 2030 there will be more than 65 million obese people in this territory (Wang et al, 2011; Nongmaithem et al, 2016). Thinking in this way, great pressure is expected on the healthcare system when it comes to chronic wounds such as diabetic foot ulcers.

Some of the limitations of this research, in addition to the fact that the sample is quite small, is that the localization of diabetic foot ulcers was not recorded, while the findings of other studies indicate a dominant plantar localization of these changes with a frequency of 58.3% (Bekele et al, 2019). Also, the limitation of this study was the measurement of the depth of the ulcer, which cannot be declared as a completely reliable measurement due to the different appearance of each observed diabetic foot ulcer, but also that we did not monitor the healing process according to the $cm^2/week$ formula.

CONCLUSION

This research did not prove a connection between the diameter of the ulcer and BMI, while when we talk about the depth of the ulcer, we see a positive dynamic in relation to BMI values, although without statistical significance. Also, there is a certain positive dynamic of BMI with clinical outcomes of diabetic foot ulcer treatment, but without statistical significance. Diabetic foot ulcer is ultimately a complex problem, where it is very difficult to say to what extent obesity is the cause, and to what extent it is the consequence of the disease.

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Received: May 20, 2023

Accepted: June 30, 2023



DOI: 10.7251/QOL2303130J

UDC: 616.728.2-089.28:617.581-77-06

Paper review

COMPLICATIONS IN PRIMARY TOTAL HIP ARTHROPLASTY

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ABSTRACT: Primary total hip arthroplasty is a surgery during which an orthopedic specialist removes damaged parts of hip and replaces them with parts usually built from metal, ceramics and very hard plastic. Modern technology, materials of good quality and an advanced operative technique enable quick postoperative recovery and total disappearance of pain that was present before the operation. Despite all preoperative and postoperative measures applied, some complications may occur, these include: infections, luxations, periprosthetic fractures, implant allergy, psoas impingement, deep vein thrombosis, neurological complications, allergy to metal implants as well as fatal outcome.

Keywords: complications, hip arthroplasty.

INTRODUCTION

Complications in primary total hip arthroplasty are the following:

- Infections
- Luxations
- Periprosthetic fractures
- Implant allergy
- Psoas impingement
- Deep vein thrombosis
- Neurological complications
- Allergy to metal implants
- Fatal outcome

INFECTIONS

Perioperative infections are among the most common complications in orthopedic surgery, complications that cause the greatest fear as far as the outcome of treatment is concerned. They are currently the leading cause of failure of primary and revision hip and knee arthroplasties (Bozic et al., 2010). Periprosthetic infection is a catastrophic event for patient and a frustrating problem for surgeon. Unlike dislocation which is an instant problem and requests a quick solution, an infection is a long lasting, exhausting problem that causes prolonged stress reaction in patient and surgeon.

The beginning of this century and millennium was marked with a "biological big bang" in arthroplasty. A change in paradigm came about. The majority of great problems of mankind are biological, hence the solutions will be biological. What physics was in the 20th century, biology will be and already is in the 21st century. While the major problem of the 20th century in arthroplasty was tribology, in the 21st century it is biology. Periprosthetic infections are a typical example of biological problem that requires biological intervention. These infections are diagnostic, therapeutical and economical problem. They are biofilm infections and represent one of the most complex problems in the context of implants. It has been argued

in more recent publications that these infections are third by frequency of complications after total hip arthroplasty, percentage wise 0.3-2.2 %. With increase in the number of hip arthroplasties, an increase in number of these infections is expected as well. Also, increase in percentage from 1.4 to 6.5 % is predicted (Usbeck & Scheuber, 2014).

Presence of foreign material increases pathogenicity of bacteria. Infections associated with implant develop in the presence of a small number of bacteria (e.g. 100 *S.aures* bacteria). The most common causes of these infections are coagulase-negative staphylococci (30-43 %), *Staphylococcus aureus* (12-23 %), mixed flora (10-11 %), streptococci (9-10 %), Gram-negative bacteria (3-6 %), enterococci (3-7 %) and anaerobes (2-4 %). High degree of microbial diversity requires microbiological identification, and an empirical therapy without it must be avoided (Ochsner et al., 2014).

Periprosthetic infection classification:

- Early infections (0-3 months). These infections are mostly caused by a very virulent pathogen such as *S.aureus*.
- Postponed infections (3-24 months). These infections mostly occur intraoperatively and include poorly virulent pathogens such as coagulase-negative staphylococci.
- Late infections (from 24 months). These infections almost always occur via hematogeneous route, most often as a result of skin infection (*Staphylococcus aureus*), respiratory tract infection (*Pneumococci*), intestinal infection (*Salmonella spp.*) and urinary tract infection (*Escherichia coli*).

An implant can be infected in three ways:

- Intraoperatively, via direct colonization of foreign material from air or from skin.
- Via hematogenous or lymphogenous transmission of pathogenous organisms from various infection foci (urinary tract, skin, lungs and other).
- Colonization can be the result of contact with neighbouring sites of infection (osteomyelitis, diabetic ulceration, hematoma and other).

Biofilm is an efficient strategy of microorganisms to improve their survival under harsh conditions such as nutrient deficiency. It is the result of adaptation of microorganisms to their surroundings. More than 80% of microorganisms in nature exist as biofilm. With the growing use of implants, medical profession is being confronted with these microorganisms that increasingly gain resistance to antibiotics.

Bacteria can exist in two forms:

- Planctonic form, metabolically active, with rapid replication.
- Biofilm-form, less metabolically active, in stationary growth phase.

Due to slow replication, bacteria in biofilms are up to a thousand times more resistant to antibiotics. A biofilm consists of 25-30 % bacteria and 70-75 % polymerized polysaccharide amorphous matrix (Ochsner et al., 2014).

A biofilm gradually develops into a complex three dimensional structure with channels (primitive circulation) and chemical communication via molecular messengers. Recent controversy is on whether this is a case of multiple microorganisms joined together or one large complex organism. Biofilm development implies the following phases:

- Adhesion,
- Proliferation,
- Maturation and
- Dispersion.

The first step in development of this infection is adhesion of microorganisms onto foreign body i.e.

the implant. This occurs due to physical and chemical mechanisms that act during the colonization. Floating planktonic bacteria get destroyed by antibodies and antibiotics, whereas adherent bacteria protected by the extracellular matrix survive. The surrounding macrophages and granulocytes degranulate and lose their phagocytic function.

Atypical variants of microorganisms so called “small colony variants” can develop in close proximity to the implant. This subpopulation of staphylococci or other bacteria (*Pseudomonas*, *Escherichia coli*) have even slower degree of replication and growth, atypical morphology, and reduced metabolism. The phenotype is associated with even higher ability of biofilm formation which enables persistent infection. They are also resistant to antibiotics and therefore called “difficult-to-treat” bacteria.

Preoperative malnutrition is recognized as an independent risk factor for this infection. Besides, these patients receive more transfusions and as such, they are at a higher risk of an infection.

An increased risk of hip implant polymicrobial infection after front mini-invasive approach has been confirmed by research. Lateral approach which is further away from the groin is more recommended, especially in obese patients.

CLINICAL SYMPTOMS AND DIAGNOSTIC PROCEDURE

Acute pain, redness in wound area, swelling, warmth, increased temperature are classic signs which could indicate development of reinfection. Secondary secretion from wound, hematoma, increased inflammation parameters (secondary increased CRP) must be recognized in time. If an active surgical intervention is late by 3 weeks, a fistula usually forms and the infection can then be treated only by explantation of implant.

Signs of a postponed infection are fistulae, abscesses, nonspecific symptoms such as permanent postoperative pain and subfebrile. Symptoms of a late infection are often similar to those of an early infection. The greatest risk of a hematogenous periprosthetic infection is septicemia associated with *S.aureus*. Unfortunately, no single laboratory test (CRP, ESR, LE, procalcitonin, interleukin-6 or others) can confirm nor rule out a periprosthetic infection with certainty. Arthrocentesis is the key type of analysis. A good level of sensitivity and specificity is present in leukocyte counting from synovial fluid and in determining granulocyte percentage. Sensitivity of a culture to antibiogram is variable, especially if antibiotics had already been given.

Sonication method has the greatest sensitivity, especially if performed prior to antibiotic therapy.

X-ray imaging can show osteolysis around implant along with bone remodeling which are often also associated with aseptic processes. This diminishes the specificity of radiological signs. However, a classic X-ray image shows well the bone structure, whereas changes can be detected by comparison with earlier X-ray images. In an X-ray image there are no metal artifacts. The primary weakness of X-ray imaging is poor insight into soft tissues, fistulae and abscesses.

CT imaging also has its advantages:

- Short imaging period
- Good bone structure display
- The best sequester display
- Multiplanar reconstruction
- Absence of claustrophobia (compared to MRI)

And disadvantages:

- Relatively poor display of soft tissues
- Metal artifacts

- **Radiation**

Magnetic resonance imaging (MRI) can not be applied on patients with ferromagnetic implants. MRI can show changes in soft tissues better than X-ray and CT imaging. It is also better for visualization of anatomic details compared to scintigraphy. MRI shows acute inflammation, abscesses and fistulae with high sensitivity and specificity. On the other hand, specificity of the MRI is diminished in case of a chronic infection and there is no differentiation between a chronic infection and a reparative scar.

Ultrasound examinations can be used in locating joint effusions or as a control during puncture and drainage of a joint.

Scintigraphy provides functional diagnosis of bone metabolism. Concentrations of radioactive substances necessary in scintigraphy are significantly lower in comparison to contrast MRI and CT diagnostics. This group also includes PET/CT imaging.

Collection of microbiological samples requires a prior two week suspension of antibiotic therapy.

Histological testing and examination of explanted foreign bodies (sonication) are also significant diagnostic procedures in connection with periprosthetic infections.

TREATMENT ALGORITHM

The primary aim of periprosthetic infection treatment is elimination of infection and correct implant functioning.

Five different types of intervention are possible in treatment of periprosthetic infections:

- Surgical debridement with retention of implant,
- “One-stage” revision,
- “Two-stage” revision with use of a spacer,
- Explantation of implant without reimplantation (“hanging hip”),
- Suppressive long-term antibiotic therapy without surgical intervention.

ANTIBIOTIC THERAPY

Prior to introduction of antibiotic therapy, it is necessary to verify bacteria and its degree of resistance. Antibiotic therapy is defined well and clear for the case of periprosthetic infection by staphylococcus. Rifampicin should be given in combination with quinolones (ciprofloxacin, levofloxacin). An oral therapy with penicilins and cephalosporins is not recommended, neither is a monotherapy with rifampicin nor with quinolones against staphylococci (Ochsner et al., 2014).

PREVENTION OF PERIOPERATIVE INFECTIONS

Prevention of perioperative infections can be preoperative, intraoperative and postoperative.

Preoperative prevention:

- If patient has either systematic or local bacterial infection, then it must be treated and the elective surgery postponed.
- If patient has diabetes, the blood glucose level must be under optimal control.
- The risk of infection is increased in patients who smoke.
- Washing with antiseptics before operation lowers density of microorganism colonies on the skin of patient. Research, however has not succeeded to confirm significant reduction in the rate of infection. Therefore, duration and the way of decolonization are not yet based on evidence.
- Before first operation, surgical team should wash hands such that no visible uncleanness is present.
- Surgical team must disinfect hands by an accepted routine procedure. The procedure must be

fixed without changes. Artificial nails are not allowed.

- Hands are disinfected before every next operation.
- Patient's skin in surgical field area must be washed, then manually cleaned.
- Shaving of surgical field is done right before the operation if possible.
- All staff in operating theatre must be vaccinated against hepatitis B.
- Staff must be reporting about eventual transmissible diseases.
- Preoperative stay in hospital should be as short as possible.

Intraoperative:

- Patient must be well oxygenated and must not be hypothermic.
- Doors on operating theatre must be closed, or their opening should be as rare as possible.
- Surgical masks, coats and gloves still have an irreplaceable role in infection prevention, and advancements in their making are necessary and possible.
- Surgeon needs to change gloves prior to insertion of definitive implant even though there is no strong evidence for this recommendation.
- Surgeon can lower the risk of infection if there is maximum respect for patient, respect towards tissue, atraumatic technique, meticulous hemostasis, ability to estimate which tissue should be saved and which should be removed.
- Drains are let out through special incisions distant from operative wound. The use of closed drainage systems is compulsory. A recent practice that does not include the use of drains has been emerging whose advocates refer to quicker recovery, lower rates of infection and lesser need for transfusion. However, there is still the problem of hematoma as the base for an infection that needs to be solved.
- Only necessary staff should be in theatre during operation. "OR traffic" or motion in the theatre should be regulated without unnecessary repeats, crossings or collisions. From operator to assisting worker, everyone should be doing a strictly defined task like at a formula 1 "pit-stop". In this way preparation for operation, surgery and transport of patient from theatre will be maximally quick and effective. The old surgical saying goes: "a good surgeon operates slowly and finishes quickly". Similar meanings have language constructions "proficient surgeon" and "High Volume Surgeon".

Postoperative:

- Application of compression bandages lowers the risk of deep vein thrombosis, hematoma and infection.
- Wound dressing change is done 24h after operation by disinfected hands or wearing gloves.
- Drain is taken out as early as possible.
- Education of patient about wound care and recognizing signs of infection is necessary.

LUXATIONS

A hip endoprosthesis luxation appears in 1-3 % of primary and in up to 20 % of revision and tumorous hip endoprostheses. The risk factors are patient and surgeon (Factor patient: sex, age, diagnosis, obesity (BMI) and Factor surgeon: experience, institution, approach, implant).

Characteristics of the implant relevant to luxation are: type, components position, head size, head-neck relation, neck geometry, offset, length, fixation, design. The landmark for the version of cup is the transverse acetabular ligament. In majority of cases, it is preserved and available during operation. In the course of operation, it is necessary to perform tests on stability of prosthesis. It is impossible for a prosthesis

sis to be stable after operation if it was unstable on operating table. It is required to determine direction of dislocation, which is sometimes difficult without “opening”.

Etiology of dislocation:

- Malposition
- Abductor insufficiency
- Soft tissue or bone impingement
- Undefined

Dislocation treatment can be nonoperative or operative. It is difficult to determine the borderline of when to give up with nonoperative and to indicate operative treatment. An operative treatment is reserved for non-readjustable, luxation prone and multiple luxated prostheses.

Luxation of total hip endoprosthesis is the most common reason for operation after primary arthroplasty. Preoperative planing and preparation are required for operation success. It is necessary to identify and understand the problem before the actual operation. A smaller mistake in the version of acetabular component can be corrected with change from a standard to an asymmetric insert. As far as the inclination of cup is concerned, it must not be less than 30 degrees. Soft tissue and bone impingement must be solved by additional debridement of soft tissue and bone resection on the edges of acetabulum. Based on results of numerous studies, optimal position of acetabular component is 45 degrees inclination and 20 degrees anteversion.

Correct implant position is the best dislocation prevention after operation, which is the most common early complication after total hip arthroplasty. It is a huge problem for patient and surgeon. The patient is dissatisfied, clinical results are worse, and additional treatment costs are significantly higher. A large number of dislocations require repositioning in general anesthesia or even reoperation.

The main cause of dislocation is malposition of implant components, whereby malposition of acetabular component is by far more frequent cause of dislocation in comparison to femoral component.



Picture 1. X-ray images of luxated total endoprosthesis

Correct orientation of acetabular component is also of crucial importance for the range of motion after surgery. This finding is clinically significant since many surgeons strive to reduce inclination of acetabular cup in hope of increasing stability. Reduction in angle of inclination below 30 degrees causes impingement with flexion which leads to subluxation or dislocation even when the cup is adequately anteverted. Mistakes that occur during placement of acetabular component can not be compensated with correction of anteversion of femoral component.

Correct position of implant extends the lifetime of implant. If the position is incorrect, this increases

pressure on additionally strained zones of acetabulum which causes friction and wear on the polyethylene cup. Irregular kinematics and irregular arrangement of active forces leads to faster wearing of implant and bone tissue in additionally strained places.

One of the future aims is to produce such an implant that will preserve kinematics aligned with other kinematic chains in organism and significantly improve life quality of patient.

PERIPROSTHETIC FRACTURES

Periprosthetic fractures are a complication that can significantly compromise the result of operation. If they occur during operation, this changes the plan of operation and extends its duration. If they occur after operation, the plan of rehabilitation gets changed, its duration prolonged, and most often a new operation is necessary.

Diagnosis of this type of fracture is sometimes quite difficult and oversights are also common. In that case, a look at postoperative X-ray image causes big surprise and frustration in surgeons. Therefore, it is important to consider the possibility of occurrence of this complication. This way, the surgeon can “see” it before it “sees” him. The risks for occurrence of periprosthetic fractures are: cementless fixation, minimally invasive surgery, female sex.

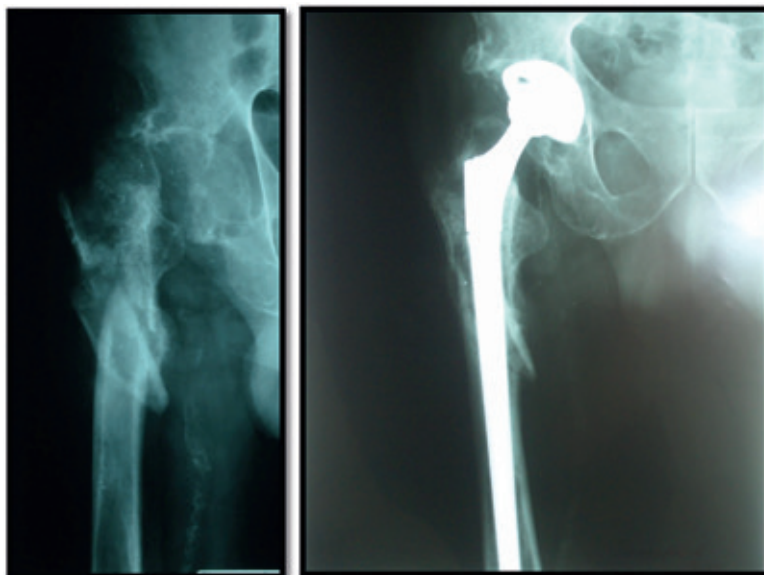
It is necessary to estimate fracture and implant stability, then determine the way of treatment and the type of operation accordingly. The options for operative treatment are revision arthroplasty and/or open reposition and internal fixation. Decision about the type of revision surgery is influenced by: fracture localization, stem stability, bone mass quality and patient’s general condition.

Modular revision stem implies distal cementless fixation and modularity of endoprosthesis’ neck. Monolithic cylindrical stems, “megaprotheses” and Wagner stem (often applied in Europe) have higher risk from stress shielding and descending.



Picture 2. Modular cementless revision stem (Source:Internet)

Iatrogenic fractures occur due to inadequate approach and operational technique, stem malposition, cortical osteolysis or damage to calcar and lesser trochanter. Postoperative fractures occur mainly as a consequence of falls and other types of accidents. Postoperative periprosthetic fractures of femur occur in less than 1 % of primary hip arthroplasties and in between 1.5 % and 18 % of revision hip arthroplasties (Wendy et al., 2017).



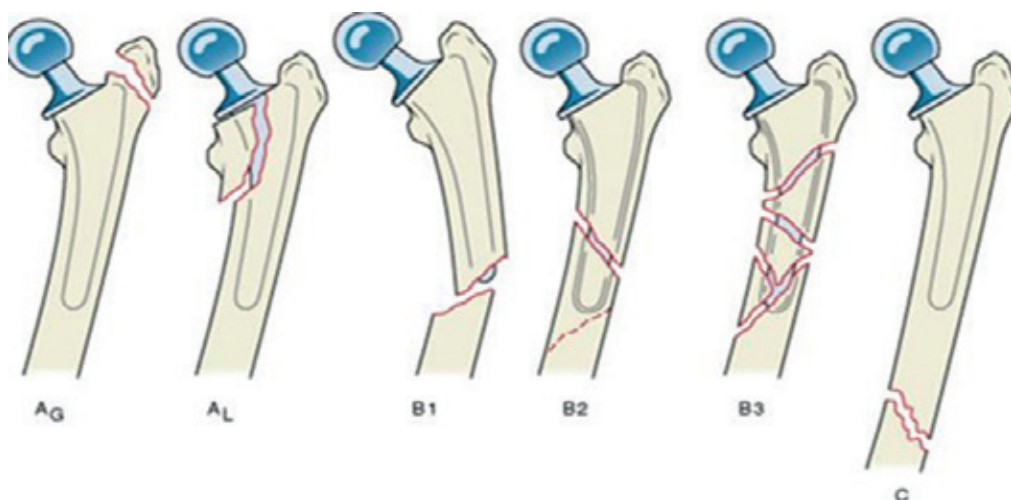
Picture 3. Preoperative and postoperative images of a periprosthetic fracture B3 type treated in two acts due to infection (Source: author's personal archive)

There are algorithms in treatment of these fractures, however it is sometimes required to make changes to these due to the individual parameters. It is necessary to know and to have a wide palette of tools and techniques available to solve every individual periprosthetic fracture.

Types:

- Simple and complicated
- Intraoperative and postoperative
- Cement and cementless
- Perforations, longitudinal and dislocated

In classification of these fractures, the most commonly used is Vancouver classification. It defines place of fracture, stem fixation quality and bone quality.



Picture 4. Vancouver classification of periprosthetic fractures – Scheme (Source:Internet)

Type A: Fracture at trochanter level; Type B1: Fracture around stem or directly below with good stem fixation; Type B2: Fracture around stem or directly below, stem loosening, with proximal bone kept in good condition; Type B3: Fracture around stem or directly below with poor quality proximal bone, multiple proximal fractures; Type C: Fracture below the prosthesis (stem) level.

The goal of surgical treatment is to provide:

- Fracture stability
- Implant stability

IMPLANT ALLERGY

Materials for osteosynthesis and artificial joint replacements – especially artificial hip and knee joints – are installed in more than 300 000 cases annually in Germany alone. In case of complications, mechanical causes and infections are mainly suspected on.

Prevalence of allergy symptoms due to metal implants is less than 0.1 %. Skin reaction to metals is frequent, however reactions of deep tissues to metals are rare. Association between skin hypersensitivity and clinically relevant reactions from deep tissues is not clear. There is still lack of reliable epidemiological data about hypersensitivity to orthopedic implants. In Germany, there is a register for hypersensitivity to implants where information on patient characteristics and long term results after revision operation are stored.

Corrosion and abrasive particles lead to release of metal. In that context nickel, chromium, and cobalt as well as occasionally components of bone cement are described to cause allergy to implants (type IV allergic reactions). Increased rates of allergies to metal (nickel, chromium and/or cobalt) were recorded in hip arthroplasty patients of old generation (1975 – 1990) in metal-metal arthroplasty (e.g. McKee-Farrar) or in metal-to-plastic arthroplasty (Charnley). A study published in 2005, was comparing patients of hip arthroplasty (ceramic, metal to plastic, metal to metal), of whom 53 had stable and 104 loosened hip replacements. The study showed that allergies to metal or bone cement were not directly associated with implant failure, but with worse ten-year survival rate of implant, (41.3 % compared to 50.5 %).

PSOAS IMPINGEMENT

Incidence of psoas impingement after total hip arthroplasty (THA) is even 4.3 %. Although psoas muscle can be irritated by bolts for acetabular fixation that penetrated through iliac bone, the most common place of iliopsoas impingement is located on the front rim of acetabulum. This could be caused by squeezing out of cement and / or by acetabular component sticking out, or by armature ring that is either too large for native acetabulum or is in reversed or side position. Irritation of psoas after THA can also be caused by reasons other than impingement with movement, such as increased motion or significant leg lengthening.

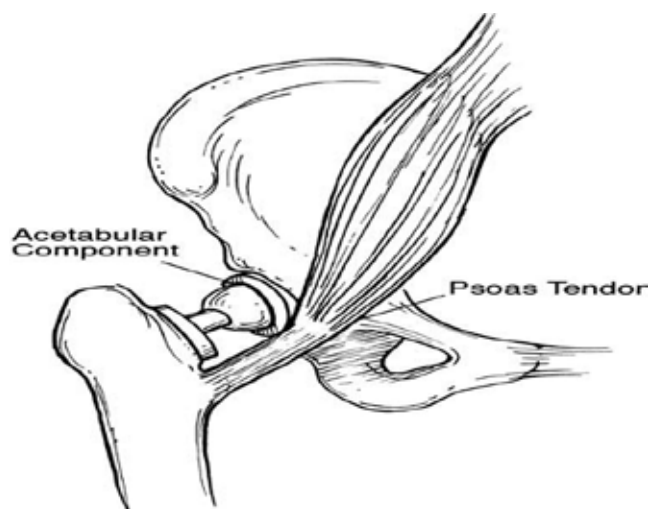
Iliopsoas impingement diagnosis should be considered in patients that report pain in the groin during activities that require active hip bending, such as walking up or down a flight of steps and leg lifting while getting in and out of car. A physical examination with careful attention to signs of psoas irritation, and visualisation of acetabular component prominence over the front aspect of rim visible from side view or from CT scans is often enough to confirm diagnosis.

Acetabular component characteristics associated with psoas impingement after THA:

- An oversized acetabular component – Researchers have identified that in comparison with asymptomatic patients, those with iliopsoas impingement after total hip arthroplasty have significantly higher difference in native femoral head diameter relative to implanted acetabular component. They discovered a 26 times higher probability of groin pain linked to iliopsoas impingement with acetabulum in patients with > 6 mm size difference of head to acetabular component.
- Acetabulum angle of inclination – It has been reported that inclination of acetabulum in coronal plane spans between 35 and 50 degrees normal, although Odri and co-workers reported 40-50 degrees as optimal range. Their research showed significantly lower inclinations of acetabula in patients with psoas impingement after total hip arthroplasty, compared to control group without

pain. The medium angle of inclination at the lowest end of normal range was - 40 ° (20-56 ° range) in those with impacted iliopsoas, in comparison with 46 ° (20-75 ° range) in those without pain. Excessive inclination of acetabulum towards down will result in greater overhang of acetabulum relative to native acetabulum, and greater pressure on iliopsoas above.

- Acetabulum retroversion – Acetabular version measured in axial plane by CT is usually greater than 0 ° and less than 25 ° anteversion, i.e. acetabular component is usually turned relatively more forward, just as an average native acetabulum. Acetabular component that is in retroversion (turned backward) usually results in overhanging of acetabular component towards front, predisposing psoas impingement in relation to acetabular component. Natural amount of version of native acetabulum is relevant, since Park and co-workers discovered that larger difference in anteversion between native acetabulum and acetabular component will result in greater volume of iliopsoas being exposed to acetabular component.
- Depth of psoas valley – Psoas valley or notch is a dent in the upper part of acetabular rim, between iliopectineal eminence and SIAI. Iliopsoas passes from the pelvic cavity through this dent or valley over the head of thigh bone, then to its place of insertion on lesser trochanter. This means that a certain degree of inconsistency between native and prosthetic acetabulum will occur naturally since prosthetic acetabulum is completely round, while native acetabulum has a dent at the front. This can result in relative uncovering of acetabular component at the front if psoas valley is naturally deep and if it is not taken into consideration during acetabular component placement. Kuroda and co-workers have warned about the essential importance of preoperative and intraoperative estimation of psoas valley for avoiding prominence of the front area of acetabulum relative to native acetabulum and subsequent iliopsoas impingement after total hip arthroplasty. (Picture 5.).



Picture 5. Iliopsoas and acetabular component relation. Accessible at: [https://www.arthroplastyjournal.org/article/S0883-5403\(02\)00229-2/fulltext](https://www.arthroplastyjournal.org/article/S0883-5403(02)00229-2/fulltext)

DEEP VEIN THROMBOSIS (DVT)

Deep vein thrombosis (DVT) occurs with formation of a blood clot in one of the deep veins inside body. It can happen if the vein becomes damaged or if the blood flow inside slows down or stops. Although, there is a number of risk factors for progress of DVT, two most common are lower body part trauma and operations which include hips or legs. DVT can have serious consequences. If blood clot gets released,

it could travel with blood stream and block the blood flow to lungs. Although it is rare, this complication known as pulmonary embolism could be fatal. Even if the blood clot does not get released, it could lead to permanent damage of vein valves. These damages can lead to longlasting leg problems, such as pain, swellings and ulcers on legs. In many cases, DVT occurs without apparent symptoms and is very hard to discover. Consequently, medical practitioners focus on preventing development of DVT by applying various types of therapy, depending on the needs of patient.

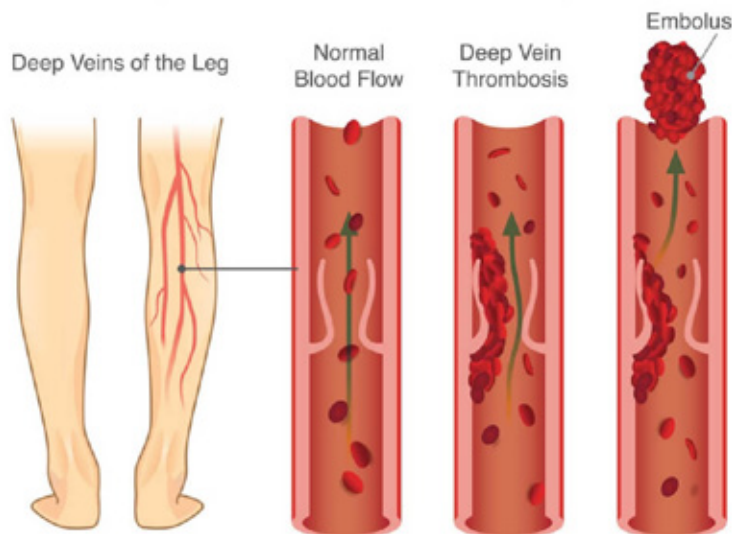
Three primary factors contribute towards development of blood clots in veins (Virchow triad): slowed down blood flow, hypercoagulability and vein damage.

- Slowed down blood flow (stasis) – Walls of veins are smooth. This helps in free blood flow and mixing with natural agents (anticoagulants) in blood which prevent blood clotting. Blood that does not flow freely and mix with anticoagulants has higher probability for blood clot formation. Therefore, it is important to watch out for signs of DVT in people who are resting in bed, immobilized in splint or plaster cast, or unable to move for longer periods of time.
- Hypercoagulability – Blood clots or coagulates around matters that do not belong to veins. Matters like tissue debris, collagen or fat can get released into blood system and cause blood coagulation during operation. Besides that, bone preparation for accepting prosthesis during total hip replacement can incite the body to release chemical matters called antigens into the blood system. These antigens can also encourage clot development.
- Damage to the walls of veins – Medical practitioner has to relocate or pull soft tissues, muscles or tendons during surgery to be able to approach the area to be operated on. This can in some cases release natural substances that encourage blood clotting.

Without prophylaxis, DVT occurs in 80 % of cases after THA and in 10 - 20 % of cases, occurrence of PE is present. With prevention, only just 0.4 % of cases exhibit occurrence of DVT with primary THA and 0.7 % of cases with revision surgery, while PE occurs in 0.3 % of cases with primary THA and in 0.4% of cases with revision THA.

Although DVT can occur in any deep vein, it most often occurs in pelvic, upper leg and lower leg veins. A number of factors can affect the blood flow in deep veins and increase the risk of occurrence of blood clots. This includes:

- older age, pregnancy, obesity,
- personal or family anamnesis of DVT or pulmonary embolism, inherited coagulopathy,
- cancers,
- vein disease, such as varicose veins,
- smoking and
- use of contraceptive pills or hormone therapy.



Picture 6. Illustration of DVT. Accessible at: <https://www.sonashomehealth.com/what-is-deep-vein-thrombosis/>

Syptoms of DVT occur in leg affected by blood clot and include:

- Swelling,
- Pain and sensitivity,
- Distended veins,
- Red or discolored skin and
- Hard or thickened veins.

However, many patients have no symptoms at all. In some cases pulmonary embolism can be the first sign of DVT. Symptoms of pulmonary embolism include:

- Shortness of breath,
- Sudden chest pain,
- Coughing and
- Expecterating or vomiting blood.

Most often applied guidelines for DVT prophylaxis after arthroplasty are guidelines of American College of Chest Physicians (ACCP) (2012) and American Academy of Orthopaedic Surgeons (AAOS) (2011). ACCP recommends the undertake of pharmacological prophylaxis in THA and TKA, with 1B degree recommendation for low molecular heparins, fondaparinux, dabigatran, apixaban, rivaroxaban, unfractionated heparin, vitamin K antagonists and aspirin, minimum 10-14 days and up to 35 days. They recommend use of low molecular weight heparin relative to other agents (2C/2B degree recommendation). AAOS recommends use of pharmacological agents for prophylaxis in THA and TKA for as long as patients have no increased risk of bleeding, however they do not recommend any particular agents. The bottom line is that orthopaedic surgeons have to find a balance between increased risks for unwanted events that more powerful pharmacological agents impose, and risk factors for DVT in each patient. One of the criticisms of current guidelines is towards their inability to give recommendations at the individual patient level. Globally, adherence of suppliers to guidelines is relatively poor, but it is an improvement; it has been recommended that adherence perhaps could be improved further if the guidelines become able to provide advice at the individual patient level.

NEUROLOGICAL COMPLICATIONS

Reported incidence runs from 0.08 % to 7.6 %. The incidence in primary THA runs from 0.09 % to 3.7 % and in revision THA from 0 % to 7.6 %. Reported etiologies include intraoperative injury to the

nerve directly, significant leg lengthening, improper retractor placement, extravasation of cement, thermal damage associated with cement, positioning of patient, manipulation and postoperative hematoma.

The total frequency of nerve injury after THA is estimated to be around 1 %. Pareses of sciatic nerve make up 79 % of all cases, followed by pareses of femoral nerve (13 %), combined paresis of femoral and sciatic nerve (5.8 %) and paralysis of obturator nerve (1.6 %). In most cases (47 %), etiology is unknown. Other causes include pulling (20 %), contusion (19 %), hematoma (11 %) and dislocation (2 %), along with laceration which makes up only 1 % of all nerve pareses. Risk factors for nerve injury include female sex, revision surgery and developmental dysplasia of acetabulum.

When the sciatic nerve is affected, it most often includes common peroneal component. It is considered to be due to smaller amount of connective tissue present between the nerve and its relatively bound position in comparison to tibial branch. It is considered that these factors make peroneal branch more susceptible to trauma and pulling. Application of the rear access is traditionally associated with increased risk of sciatic nerve damage. However, Cochrane's examination from 2006, did not establish a difference in frequency of nerve paralysis between rear and direct side approach. Paralysis of femoral nerve is rarer and often secondary in relation to direct compression, usually as a result of incorrectly placed retractor.

Indications for surgical intervention in patients with nerve paralysis include hematoma which is causing compression, paralysis associated with excessive lengthening and paralysis that can be definitely assigned to implanted metal construction. Electrodiagnostic studies can be useful in determining the level of lesion. Outcomes of nerve paralyzes are variable, 40 % of patients show good recovery, 45 % have mild residual motor or sensory symptoms and 15 % show intense motor or sensory deficiency. Partial nerve lesions and some motor function maintenance are good prognostic indicators, with possibility of recovery in up to 3 years since the start of injury.

CLAUDICATION

Claudication as a complication after total hip arthroplasty occurs relatively rarely. In some works it is associated with lateral approaches and abductor insufficiency (m. gluteus medius). Just like inequality, it can be a reason for dissatisfaction of patient if the patient was not familiar with it before the operation.

INEQUALITY

Unequal length of lower extremities after total hip arthroplasty is a common and known complication that can be a reason for dissatisfaction of patient. It is also the most common reason for lawsuits against orthopaedic community.

Besides elimination of pain, restoration of the biomechanics of hip joint is also an important goal in total hip arthroplasty as it enables a normal walk and support. Key components of a successful hip arthroplasty are:

- Achievement of correct centre of rotation,
- Neat position and orientation of components,
- Adequate offset and
- Equality of lower extremities.

Lengthening of operated leg is a more common case than shortening. The incidence of inequality in literature has a wide span, from 1 % to 27 %. The length span is same, from 3 mm to 70 mm.

The cause of inequality is multifactorial. Surgical goals during operation are multiple and the most important is stability of prosthesis. These goals are sometimes in conflict, and in the end surgeon has to choose "lesser evil", in other words inequality in order to gain stable prosthesis with neat range of motion

and good function. It is sometimes necessary to extend the neck so that soft tissues would get tightened and stability improved all at the cost of leg lengthening.

Informed acceptance by the patient is of great importance in this situation. Inequality has to be discussed as a possible complication. Discussion must be documented. It is also necessary to preoperatively measure lengths of lower extremities to be able to determine if it is real or apparent shortening of extremity.

It is almost impossible to measure lengths of legs intraoperatively if patient is in lateral decubitus. Critical moments during surgery are determining the level of neck resection, length of neck and femoral offset. This clearly points out the fact that a single component or prosthesis is not a fit for all patients. Inequality is commonly associated with pain in the lower back section, walking disorder, dislocations, component loosening and great dissatisfaction in general. Everyone is unhappy and extremely desperate including surgeon.

Without doubt, inequality as a complication can not be eliminated in total hip arthroplasty. The boundary between acceptable and unacceptable inequality is for now undefined. Some studies show good tolerance of 1 cm difference in leg length by the majority of patients.

On the other hand, patients detect with out error even smallest lengthening of leg and are mostly unhappy if they have to carry an elevation in the contralateral shoe.

Greater lengthening of operated leg can turn great clinical results in terms of pain release, range of motion, and function of hip into surgical failure due to dissatisfaction of patient.

Techniques used to achieve equality in lower extremities during total hip arthroplasty are divided into three categories:

1. Preoperative "templating".
2. Intraoperative techniques with femoral and pelvic markers.
3. Complex mathematical calculations.

In this way, the incidence of this complication can be at least lowered if not completely eliminated.

CORROSION OF TAPER

The focus on taper corrosion was attracted by problems with the application of metal-metal in large head component to standard stem. Corrosion associated problems have been noticed in modular primary stems as well. Mainly used in Europe today is "euro taper" or "12/14" taper. It is important to highlight that taper dimensions have not been standardised so far and vary between manufacturers. Factors that influence occurrence of taper corrosion:

- Design and material,
- Surgen factor (position) and
- Patient factor (burden).

Combination of CoCr head and titanium stem results in occurrence of Co and Cr debris and corrosion process (Morlock et al., 2020).

FATAL OUTCOME

Life in itself is enough complicated. Death as an inevitable part of life makes it even more complicated. Fatal outcome as a complication in total hip arthroplasty can not be eliminated totally.

The authors have recorded mortality from 0.35 % in the first 30 days after total hip arthroplasty. Male patients, people over 70 years of age and patients with cardiac and renal diseases are at a higher risk of a lethal outcome.

CONCLUSION

In the past three decades, total hip arthroplasty has become one of the most common operational undertakings in orthopaedic surgery. By the number of implanted large joint endoprostheses, implantation of hip endoprosthesis is in the first place. The most common early complication after hip arthroplasty implantation is luxation. Postoperative infection in joint alloplasty is one of the most difficult complications that often requires a quick operative treatment. Treatment is comprised of incision and evacuation of purulent content. If it is a case of an infection followed by increased temperature, increased SE and CRP accompanied with signs of septic state, it is necessary to remove the arthroplasty. Occurrence of extensive hematomata after hip operation is also a state of emergency that requires operational treatment in terms of hematoma evacuation to prevent further complications, primarily infection. An arthroplasty trunk fracture is one of the most difficult late complications in joint arthroplasty that requires urgent operational treatment in terms of endoprosthesis exchange. Although, state of emergency in hip endoprostheses are relatively rare, it is important to recognize described complications and to surgically take care of them as urgently as possible.

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Received: November 7, 2022

Accepted: March 30, 2023



DOI: 10.7251/QOL2303146S

UDC: 615.32:633.88]:582.975

Paper review

PHYTO THERAPEUTIC IMPACT OF MEDICINAL PLANTS; A REVIEW

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ABSTRACT: Medicinal plants play a major role in the development of human cultures. Medicinal plants are a rich source of phytochemical compounds, which have proven therapeutic efficacy throughout the ages. The therapeutic efficacy is attributed to those secondary biologically active compounds. Plants have provided the human being with all his needs of food, drink, and clothing. In addition they are an important source for the treatment of many diseases being the basis of the science of alternative medicine, In recent times, the area cultivated for these medicinal plants has increased, and scientific research has tended to study the effectiveness of these plants in treating many diseases. Most plants have an effective effect as an antioxidant, anti-hyperlipidemia, hypoglycemic, antihypertensive as well as for cardiovascular diseases and strokes. The study aims to provide important data on the extent to which some medicinal plants are used in the treatment of various diseases.

Keywords: Medicinal plants, Traditional medicine, Antioxidant, Diabetes, Hyperlipidemia, Hypertension, Secondary metabolic.

INTRODUCTION

Natural products extracted from medicinal plants have been used to treat many diseases. Since the dawn of history, medicinal plants have been the first source of treatment due to their availability, ease of access, low cost and side effects compared to chemical drugs. According to a report by the World Health Organization, nearly 80% of the population of developing countries around the world use medicinal plants to treat their various diseases. Cultivation of medicinal plants helped provide an important source of biological compounds. And medicine in the modern era still relies, like alternative medicine, in relying on medicinal plants in treatment. Where, the plant works to produce secondary metabolites, which are phytochemical dumps that have a high ability not only to protect the plant, but also to protect humans and animals from pathogens. There are many phytochemical compounds such as phenols, polyphenols, alkaloids, saponins, terpenes, and flavonoids. These compounds have antioxidant, antiviral and antibacterial activity, antihypertensive and antidiabetic activity (Vivek-Ananth et al., 2023).

Currently, oxidative stress plays the major role in the development of wide range of disorders. Oxidative damage due to reactive oxygen species occurred due to impaired balance between the antioxidant molecules to neutralize and the production of ROS and RNS (Kalim et al., 2010). The molecules act as antioxidants reduce or prevent the oxidation of the substrate. Oxidation reactions lead to free radicals that start the chain reactions and can then induce many human diseases (Chatha et al., 2014). Antioxidants neutralize the free radicals leads to chains reactions and self-oxidized to prevent the chemical changes in biological molecules (Halliwell, 2005). Although, in routine free radical or ROS involved in the production of energy,

but these do not only cause oxidative damage to proteins, nucleic acids and lipids; also have an important role in the disruption of intracellular signaling and phagocytosis. Oxidative damage may cause a wide range of contagious diseases like diabetes, obesity, aging, cancer, cardiovascular diseases, joint disorders, and Alzheimer's disease (Bergamini et al., 2004; Afonso et al., 2007; Chatha et al., 2014).

ANTIOXIDANT ACTIVITIES OF PHYTOMOLECULES

Different enzymes include catalase, superoxide dismutase and glutathione peroxidase in our body acted as natural antioxidant defense to eliminate the free radicals (Dharani and Kalaivani, 2015). Catalase finally produces the water and oxygen molecules from superoxide produced during the metabolic reactions (Kefer et al., 2009). Phenolic compounds such as polyphenols, found in plants play a major role in pharmacological and many biological activities like antioxidants, anti-allergic, antimicrobial, anti-inflammatory, cardioprotective, anticarcinogenic and vasodilatory effects, etc. Many plants with medicinal value are rich with active metabolites, flavonoids, phenolic acids and terpenoids. These active plant metabolites are useful in the scavenging of free radicals, metal chelating and the reduction of single tone oxygen (Shan et al., 2007; Gromovaya et al., 2008; Koukoui et al., 2015; Zahin et al., 2016).

PHYTOCHEMICALS AS ANTIOXIDANTS

Experiments have shown that medicinal plants are rich in antioxidant compounds such as phenols, carotene, and tocopherols. These plants produce huge amounts of these biologically active compounds that protect against free radicals. In addition to containing some minerals such as A, C, and E, which act as antioxidants. Where, these compounds control the inhibition of oxidation resulting from reactive oxygen species (ROS), affecting the dynamics of the interaction, leading to a delay in aging and the treatment of many cancers. Therefore, it was recommended by the World Health Organization and institutions concerned with human health that these plants should be used effectively (Michalak, 2022).

The compounds that contain all the chemicals in the human body are called phytochemicals. Several types of plant metabolites such as saponins, flavonoids and tannins have been studied in *Conisa sumatriensis* (Shah et al., 2012). Common metabolites such as tannins, saponins, flupatanins, terpenoids, steroids, glycosides, and flavonoids were found in phytochemical evaluation of plant. ...

Prophylaxis of diterpenoid tumors associated with *Cladonia rangivirina* has been reported. Plants, leaves, roots, flowers and natural resources are important sources of medicinal plants. The flavonoids and phenols of seven medicinal plants from different families were found. *Oldenlandia corymbosa*, *Xanthium strumarium*, *Ricinus communis*, *Terminalia bellirica*, *Tinospora cordifolia*, *Ipomea aquatica*, and *Bryophyllum pinnatum* are found in these plants (Yadav and Agarwala, 2011). The compounds of plant origin prevent hepatitis B by stimulating the immune system. Silymarin, sitosterol, neoandrographolide, philine, curcumin, picoside, betaline, andrographolide, hypophylline, glycyrrhizin and cocoside due to their hepatoprotective properties may be under stimulation of flora (Asadi -Samani et al., 2011).

The phytochemicals from *Bauhinia hookeri* includes corrosive bile, tricyclic procyanidin, corrosive secondary hydroxydynamic, flavonoids have hepatoprotective effects. Phytochemistry plays an important role in plant conservation. There are often many compounds and plants capable of fighting free radicals. Atomic polyphenols have been studied because they are commonly used in food supplements and play an important role in free radical testing for the treatment of liver disease (Rehan et al., 2014).

The protective effect of plants on the liver is due to anticancer and anti-inflammatory properties (Nithianantham et al., 2011). It has also been found that the formation of cell support compounds is stronger than a single component. Cancer inhibitors are drugs commonly used for the combination of phenols and

flavonoids, indicating that Ipomoea potatoes are a major source of normal cell proliferation that can trigger a DPPH response. The relationship between non-reversible phenol levels (e.g. phenolic corrosion) and reactive pitting reactions has been described in several studies in processing plants. The anticancer properties of some active plants have also been considered, for example, *Cichorium intybus* contains the greatest source of cancer inhibitors (Rafique *et al.*, 2014). Cell-supporting phytochemicals absorb the expected protective component of the liver against paracetamol induced damage in mice (Gyawali *et al.*, 2017).

The potential of *Punica granatum* powder for CCl₄ damage leading to cell proliferation and its protective effect on the liver has been considered. The experiments show cellular support and especially liver function. Another synthetic system that protects against free radicals is organic cells derived from vegetables. Promoting wellness and prevention combined with a healthy diet rather than a low-fat diet has a huge impact on understanding normal cell growth. Flavonoids have organic effects such as eliminating free radicals, inhibiting cell proliferation and combating oxidative stress. Many flavonoids have been shown to be oxidants, antioxidants, hepatoprotective and anti-inflammatories (Kumar & Pandey, 2013).

Phenolic compounds that often contain harmful caffeine, corrosive ferulic, and corrosive vanillin are important in preventing cancer. Several phenolic compounds are distributed in certain parts of the plant. Flavonoid aglycones (including quercetin, myricetin, kaempferol, and glycosides) are composed of flavonoids and their cellular production results from various hydroxyl reactions. The redox nature of cell optimization allows them to pursue professional reduction (Darwisd *et al.*, 2008).

A comprehensive report on the phenolic phenotype (TPC) and cellular carrier of therapeutic compounds was used. There is a positive correlation between the rate of cell proliferation and the phenolic properties of *Origanum vulgare* which has the best inhibitory capacity (Spiridon, 2011). Plant compounds are stimulated by tissue physiology and inhibit inflammatory responses. Potential studies on *Cassia auriculata* extract suggest it could be a source of cancer inhibitors. This can be used as a source of cancer prevention during the current treatment period (Gaikwad *et al.*, 2011).

The effects of anticancer medicines has been reported including a wide number of medicinal plants and their derivatives like isoflavones, flavonoids, anthocyanins, coumarin, lignin, catechins and epicatechins, which has an effect significant over zero radicals. *Camellia sinensis*, *Ocimum sanctum*, *Copipalin flute*, *Allium sativum*, *Terminalia bellirica*, *Zingiber officinale* (from the Middle East, Palestine, and India), and a certain Chinese plants and cell boosting compounds are used to treat specific diseases (Numan *et al.*, 2008).

MEDICINAL PLANTS AS THERAPEUTIC MODALITIES

Medicinal plants have been used as a source of medicine since ancient times. They used the plants as they are or after drying and grinding them. These dried parts are used either individually or as a mixture with a mixture of another plant. These plants contain biologically active compounds that are usually extracted by ethanol (Abubakar and Haque, 2020).

Since earlier civilizations, medicinal plants have been used by humans for their survival and growth. In the starting they have been food collectors and food hunters but later on depend mostly on plants. Over the years, traditional knowledge has built up the perception of plant use in food, shelter, cultivation, health care and many physical uses. Specific ways of using plants in accordance with culture, food habits and folk songs were developed for indigenous people and this data is openly transferred generation to generation (Ramakrishna and Saidulu, 2014).

Traditional medicines are key component of the tribals' therapeutic remedies and spiritual existence. WHO (2007) had estimated that the use of conventional treatments in developing countries for primary health care is 80 % and involves, in particular, the use of different extracts extracted from herbal plants

(Prasad et al., 2014). This is an indication that herbal medicinal products play a crucial role in underdeveloped countries' basic health. Identified primary and secondary metabolites develop definite metabolites. The chemical components in plant growth and production are key metabolites. Glucose and chlorophyll, essential for life, are examples of primary metabolites. Secondary metabolites do not participate directly in plant growth and are not necessary to reproduction (Elhardallou, 2011). For many other reasons, secondary plant-generated metabolites are used. It is about regulation of growth, intra and interaction and protection from infections and predators. Among the most important of these phytochemical compounds are Terpenes, Phenolics, Quinones, Polyacetylenes, Polyenes and Alkamides, Carbohydrates, Organic Acids, Alkaloids (Taid et al., 2014). Polyphenols are the most commonly used secondary metabolites that have a wide range of biological activities including antibacterial, anticarcinogenic, antiviral, hepatoprotective, cardioprotective, antithrombotic, anti-allergic, anti-inflammatory and infertility treatment (Trigui et al., 2013).

THE IMPORTANCE OF MEDICINAL PLANTS

Medicinal plants are defined as those plants that are used for treatment in alternative medicine. Medicinal plants have been used in treatment for a long time. Developing countries used it in treatment in an unorganized manner, and with the development of science, the Chinese began to use it in systematic ways. Still, traditional medicine using medicinal plants was the basis in that period, due to several things, including the high population, the spread of epidemics, the exorbitant cost of treatment, and finally the side effects of drugs chemical (Zhou et al., 2020).

The World Health Organization has indicated that the use of medicinal plants in treatment represents 25% of the population in the United States, while it constitutes nearly 80% of the population in developing countries. The most important thing that distinguishes medicinal plants is that they have no side effects or are almost few compared to chemical drugs (Zhu et al., 2019).

Plants are being used for the treatment of various disorders due to their therapeutic as well as nutraceuticals characteristics since a long time prior to the production of synthetic medicines and along with synthetic drugs. It is believed that medicinal plants are used with medicinal purposes, food and several other benefits for humankind (De Lima et al., 2015; Al-Snafi, 2016). Clinical research has shown that conventional drugs such as quinine, aspirin and morphine are all drugs extracted from plants (Butler, 2014). Organic ingredients and alternatives are therefore of considerable importance, and almost 40 percent of pharmaceutical products and their derivatives are produced from herbal plants (Lahlou, 2013). Plants have many bio-active ingredients, such as phenolics, carotenoids, flavonoids, anthocyanins, vitamins, proteins, enzymes etc. which make them a significant source for medicinal activities of plants (Lin et al., 2016).

Plants are being used for medical purposes because of limited side effects in developing countries. It is now the need of current era to explore new medicinal plants due increasing demands of natural, low-cost, safe and health promoting ability of herbal medicinal products (Hosseinzadeh et al., 2015). Herbal remedies are being used for treatment of a vast range of diseases such as skin issues, gastrointestinal complications, heart disease, nervous system problems, infectious diseases, renal problems, liver disorders as well as to manage reproduction disorders both in male and female (Sharma et al., 2014).

Even though pharmaceutical drugs are employed for treating many infectious as well as non-infectious diseases, but they are very costly with several side effects, thus it is important to seek alternative appropriate sources to resolve this problem. In this case, healthy and organic foods obtained from natural plants having abundant phytochemicals can be a hoped to provide balanced diet for a growing population around the world. Moreover, medicinal plants preparations alone and in combination are advantageous to human health (Shahidi, 2009). Taking all these aspects into consideration, this research aimed to track the

therapeutic effects of traditional medicinal plants. The following headings include a literature analysis on various areas of research work on the traditional medicinal plants.

Numerous herbal remedies in food and metabolites have been selected as the source of potential therapeutic agents (Rasmussen and Ekstrand 2014). Alkaloids, glycosides, coumarins, flavonoids, steroids, and other metabolites are among them (Sengul et al., 2011). Herbal medicine has been shown to be an effective and safe place to treat hepatotoxicity (Thirumalai et al., 2011). The plant provides a solid product that builds a system to take the branch to the next level of behavioral development and reduce damage. Rehabilitation plants are used in two ways: solid plant research to treat various diseases by agronomists and by the use of professional health experts such as (Baqar, 2001). Judges use cheap Ayurvedic herbs as an alternative to various ailments (Mahmood et al., 2003). Ordinary people also reiterate the appetite for medicinal plants and pesticides because their cultivators refuse to use them as they wish and destroy new plants that feed them (Malik & Hussein, 2007).

PLANTS AND HEALTHCARE

At the present time, the use of plants and fungi has become necessary in the medical field, as many drugs have been extracted from plants, such as aspirin, which is extracted from the willow plant. Also, shikimic acid is extracted from red anise. Also, in light of the Corona pandemic, many herbal plants were used to supply the necessary medical needs. Not only that, but the parts that are considered waste that were not used from the plant were used in industry, as *Agave sisalana* Perrine leaves were used in the textile industry (Wiesneth, 2019).

The plants are a major source of medicine for the pharmaceutical industry producing new drugs. Instructions for how to prepare it at home began about 5,000 years ago, and Egyptian papyri show many useful spices. About 224 herbs have been found in Huangdi Neijg (Chinese herbal medicine) (Hong and Francis, 2004). The drugs are expensive for everyone, so they depend on physical therapy. Many of the specimens were made from plants and produced as carriers today for use in clinical trials. Similarly, the natural properties of this useful plant are for the home industry for drug promotion (Bhattarai et al., 2008). Several investigations have revealed antimicrobial cells, potentiating and depleting cells from plants (Bokhari et al., 2013). Predictive medicine assists in prognosis, treatment and management of various diseases (Robson & Vaithiligam, 2009). Many doctors recommend painkillers, opiates, and quinine (Fabricant and Norman, 2011). In Asia and Africa, the World Health Organization (WHO) estimates that 80 percent of the world's population uses different medicines.

IMPACT OF PHYTOMOLECULES ON HEPATIC FUNCTION

Liver diseases represent a health burden on the countries of the world, as cirrhosis of the liver is the ninth cause of death in European countries. It was noted that the use of chemical drugs such as colchicine, interferon, non-steroidal anti-inflammatory drugs, and corticosteroids did not bear the required fruits in the treatment of this patient, which prompted scientists to research medicinal plants that have the ability to protect the liver. The treatment of the liver from nature was important due to its easy access and low costs. Recently, the number of people with liver disease has reached 65% of the total number of people with liver diseases (Wiesneth, 2019).

Liver plays major role in the body as the body's primary organ to regulate the body's metabolism including biotransformation and the removal of metabolized substances. It also contributes to the achievement of biochemical pathways such as energy production, the provision of nutrients, development, reproduction, and disease defense. Liver regulates the body's proteins, carbohydrates and fat metabolism, bile secretion and vitamin concentration. Therefore, healthy liver is essential for good health (Ahsan et al., 2009).

Hepatic disorders affect nearly 10% of the population seriously. Hepatitis, liver cirrhosis, hepatic steatosis, fibrosis, alcohol hepatitis and drugs induced hepatitis include most common liver diseases. It was reported that hepatotoxic substances affect the hepatic cells which form covalent links with fatty tissue and produce ROS (Raj et al., 2016). The body is continually subjected to free radicals due to certain external influences (Shanmugasundaram and Venkataraman, 2006). Antioxidants may be used as a treatment scheme to treat hepatic diseases caused by free radical exposure or oxidation (Ben Saad et al., 2021).

For the diagnosis of liver disorders, hepatoprotective medication such as rimonabant or propyl thiouracil or corticoids is used. These drugs have more costly side effects such as diarrhea, constipation, sleeplessness and depression. More cost-effective medicines with minimal side effects are therefore required (Perez-Meseguer et al., 2016). Antioxidants compounds are reported to have hepatoprotective ability in plants with medicinal value (Sanchez-Valle et al., 2012). The medicinal plants contain different antioxidant compounds particularly flavonoids which are crucial for the preventive role of plant extracts towards liver problems (Ahmed et al., 2012). Moreover, literature study have shown the antioxidant potential of plants that can be used to cure liver problems, Fig.1 (Bhandarkar and Khan, 2004; Jain et al., 2008).

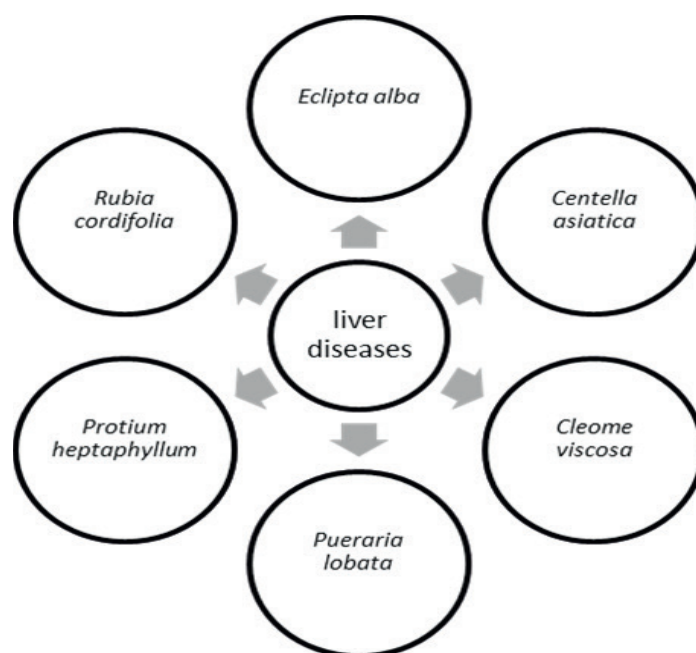


Fig. 1. Important plants family used in treatment of liver disease

The hepatoprotective capacity of cariside II was investigated on evaluating the improvement in liver transaminases in CCl_4 -intoxicated primary cultured rat hepatocytes and results revealed that $200\mu\text{M}$ administration have potential to reduce the 78% reduction in toxic effects. One of the other major flavonol glycoside as Icarin present in *Epimedium* significantly decreased the glutamic pyruvic transaminase and sorbitol dehydrogenase activities and resulting in 76% safety from toxicity at varying concentrations from $1\mu\text{M}$ to $20\mu\text{M}$. The following are widely developed ROS as byproducts of biological or exogenous factors: including singlet-oxygen (O_2), super oxide anion (O_2^-), radical hydroxyl (OH) and hydrogen peroxide (H_2O_2). These free radicals induce oxidative stress to almost every molecule present in living cells, even DNA (Sharma et al., 2001). Thus, an antioxidant mechanism must eliminate excess ROS. The occurrence of a diverse variety of phytochemical constituents plays a crucial role in the protection of hepatic injury due to the free radicals.

The hepatitis B virus (HBV) was eliminated in cell cultures in mice was managed. The effect of Osthole on both hyperlipidemic and alcoholic fatty liver animals was also demonstrated (Zhang et al., 2007; Sun et al., 2010; Du et al., 2011; Zhang et al., 2011). Mechanism studies have shown that osthole modulated multiple lipogenic gene expression (Ogawa et al., 2007), enhanced adiponectin secretion and therefore boosted resistance to insulin by PPAR α / α -activation. Anti-fibrotic osthole activities were also identified on HSC-T6 hepatic cell lines (Shin et al., 2011). ALT and AST levels are the most common used biomarkers for hepatic injury and the assessment of these enzyme activities will determine the increased or reduced intensity of hepatic lesions. After ochratoxin A (OTA) -mediated liver damage and impaired cellular membrane integrity, Jamuna et al., (2018) reported substantial increase in serum ALT, AST and LDH activities. Ameliorative group reduced serum ALT, AAST and LDH activities indicate hepatoprotective WRE impact. (Saxena et al., 2007).

Antioxidants are known to work against illnesses by reducing lipid peroxidation by breaking free radicals and raising endogenous antioxidants. Medicinally important plants contain major phytochemicals such as phenolic acid and flavonoids that are scavengers of free radicals and act as an antioxidant molecules (Cheng et al., 2011). The hepatoprotective effect of plant extracts is pre-investigated due to its antioxidant characteristics. Future studies on hepatoprotective medicinal plants can lead to safety assessments of drug detection in its early stage. Herbal medications are becoming crucial for the treatment of liver disorders in recent decades. Plant remedies are efficient and safe alternative hepatic disease treatment (Yao et al., 2016). Valuable medicinal plants can be tested to treat liver problems since medicinal products are popular worldwide (Armstrong et al., 2014). *In-vivo* and *in vitro* research on plant phenolic and flavonoids have shown excellent potential to prevent liver cirrhosis because of their high antioxidant nature.

As more than 80% of the world is dependent on conventional treatment, WHO focuses on the natural assets of medicinal and aromatic plants (MAP) as a source of disease treatment. Monitoring and categorizing MAP into its native habitats should be a strategic goal and starting “wild” plants into agriculture. As natural resources are plentiful but vary greatly, they should be monitored and tracked in typical environments (Chambers et al., 2011). Synergistic interactions between herbal or phytomedicine substances are of considerable relevance. Synergism frequently explains the effectiveness of preparation, especially in tiny dosages when it is necessary. When separated from the combination, the bioactivity or effectiveness of a component in a herbal mixture generally diminishes. It applies both to single-plant preparations and to phytomedicines that comprise more than one plant. In herbal medications, the utilization of whole or partially purified extracts containing many active components is crucial (O’Leary et al., 2001).

USE OF MEDICINAL PLANTS IN VARIOUS DISORDERS

Some important drugs (podophyllotoxin, taxol, vincristine, camptothecin) are herbicides (Komalavalli et al., 2014). Plant metabolites can alter mineralocorticoid potentials (Nithya & Balakrishnan, 2011). About 25% of these drugs are considered vegetarian in the United States, and 74% of the 119 essential drugs are packaged above traditional medicine.

Local medicinal plants are used to treat hepatitis B (Rasoul et al., 2014), various publications describe inflammatory, anti-fibrosis, anticancer and hepatoprotective effects of these medicinal plants (Brinda et al., 2012). Silymarin is used to treat gallbladder liver problems such as jaundice, hepatitis, and cirrhosis (Rainone, 2005). Several antagonists of negative growth compounds such as vinblastine, taxol, camptothecin, vincristine, subcutaneous, topotecan, irinotecan and etoposide are derived from epipodophilic toxins (Ramot and Merrion, 2008). Anthraquinone injections demonstrate several antibacterial, antifungal, anti-depressant, anti-parkinsonian, ED, antiviral and cellular functions (Zargar et al., 2011). Foods high in fats,

flavonoids and phenols may reduce the risk of several malignant tumors, including cancers of the mouth, esophagus, lung, larynx, colon, pancreas and pancreas, according to clinical studies. (Ross and Kassem, 2002). Milk thistle contains stimulants such as liver protection and growth inhibition.

Elephantopus scaber (L) is one of the most often used herbal medicines for controlling fever, as diuretics, and gastrointestinal disorders, as well as treating nephritis, nausea, edoema, pneumonia, scabies, and leukaemia. Phytochemicals of various kinds have been isolated from this plant (Wan et al., 2009).

The disease is treated with a single plant or a mixture of different spices. This herb reduces diseases such as inflammation, liver damage, rashes, fever, and stomach problems (Qureshi et al., 2007). Biological activity and damage tests have demonstrated the presence and compatibility of these plant components (Wan et al., 2009). Rhubarb is one of the most important Himalayan spices and has medicinal properties. About 60 continuous R.emodi models have been shipped worldwide. It has antiviral, antibacterial, sedative, anticancer and anticellular properties (Rahman et al., 2014). Polygonum Short provides brief links between common sites of ethnopharmacologic use, particularly for wound healing, cytotoxicity, liver injury, and protozoan disease. The leaves and heads of *Clitoria ternatea* help treat various conditions such as skin, genitourinary problems, and pain. This plant contains antidepressants, platelet inhibitors, antidiabetics, diuretics, anti-inflammatory and anti-inflammatory drugs (Bhawna and Kumar, 2010).

CONCLUSIONS

Phytochemical plays an important role in health care system. Herbal medicines are used for the treatment of various diseases. International research has proven the effectiveness of medicinal plants in treating many diseases. Where, many medical workers recommend the need to turn to alternative medicine in the treatment of some diseases that have not been proven to have been cured by chemical drugs. However, it is necessary to be careful in the use of these plants, as it cannot be considered that every natural product is safe. In addition to the possibility of some medicinal plants interacting with chemical drugs, which leads to a number of problems, and then we recommend the need to take caution when dealing with these plants, and to conduct many clinical researches to ascertain the effectiveness of these plants.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Received: February 21, 2023

Accepted: March 30, 2023



DOI: 10.7251/QOL2303157H

UDC: 159.943.072-053.2:613.25

Professional Paper

RISK FACTORS FOR OVERWEIGHT AND OBESITY IN CHILDREN AND ADOLESCENTS

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ABSTRACT: Obesity among children and adolescents can be characterized as a worrying public health problem in the 21st century. The timeline covering the last three decades records the growth of the prevalence of obesity in children and adolescents. The consequences of obesity are incalculable because they lead to many chronic diseases of the cardiovascular system, endocrinological, gastrointestinal diseases and disorders of the musculoskeletal system as well as psychological diseases. The risk factors of excess body weight and obesity are associated with the disproportion between caloric intake and physical inactivity as the main factors, and other important factors that can lead to the development of the disease (genetic, endocrine, social environment and socioeconomic factors) should not be underestimated. The aim of the work is to point out the risk factors that can lead to the development of obesity in childhood and the adequate measures for the primary prevention of this disease. Research methods. The paper used relevant literature data that indicate risk factors for the development of obesity in children and adolescents, the importance of their early detection as well as prevention measures. Conclusion. Direct the health policy towards the goal of identifying overweight children and adolescents in order to reduce the risk of developing obesity in adulthood. Prevention should include educational programs for children and adolescents with the aim of acquiring knowledge, but also changing habits related to nutrition, physical activity and lifestyle.

Keywords: children, adolescents, overweight, obesity, risk factors, chronic diseases, prevention.

INTRODUCTION

Obesity among children and adolescents (between the ages of 2 and 18 years) has increased rapidly in the last three decades of the 21st century in both developed and developing countries (1, 2). It is also alarming that around 55% of obese children become obese in adolescence. Similarly, about 80% of obese adolescents will continue to be obese in adulthood, while about 70% will be obese at the age of 30 (3). In extensive studies that included the population of children and adolescents in the time period from 1975 to 2016, they showed a trend of BMI growth. It is estimated that in 2016 worldwide, 124 million children and adolescents between the ages of 5 and 19 were obese, and 213 million were overweight (4). The World Health Organization (WHO) reports that in 2020, 39 million children under the age of 5 were overweight or obese. Considering the growth of overweight and obesity in children and adolescents, WHO member states have set a goal until 2025 to stop this negative trend and approved a project under the slogan “No increase in overweight and obesity” (5).

DEFINITION

According to the World Health Organization (WHO), overweight and obesity (obesity) is defined as abnormal or excessively accumulated fat tissue to such an extent that it endangers health and daily life (5). Health disorders caused by excess body weight and obesity include cardiovascular conditions (hypertension, hyperlipidemia), endocrinological diseases (diabetes type 2, metabolic syndrome), gastrointestinal conditions (non-alcoholic fatty liver disease), disorders of the musculoskeletal system as well as psychological disorders (depression, anxiety) (6-9). BMI (eng. Body mass index) shows nutrition as a coefficient

that is calculated through the ratio of mass in (kg) and height in meters (m) by dividing the mass by the square of the height (kg/m²). According to WHO guidelines, there are four categories of BMI for adults: underweight (BMI < 18.5 kg/m²), normal weight (BMI 18.5 - 24.9 kg/m²), overweight (BMI 25.0 - 29.9 kg/m²) and obesity (BMI ≥ 30 kg/m²) (5). Obesity is classified according to stages or degrees: 1st degree - BMI 30.0 -34.9 kg/m²; 2nd degree - BMI 35.0 - 39.9 kg/m² and 3rd degree - BMI ≥ 40.0 kg/m². To define the state of nutrition in the pediatric age group, percentile curves are used in relation to age and gender. Percentiles show the relationship between the child's BMI and the BMI of children of the same age and sex. The classification of the state of nutrition is as follows: malnutrition below the 5th percentile; normal body mass from the 5th to the 85th percentile; overweight between the 85th and 95th percentiles; obesity above the 95th percentile (10).

RISK FACTORS FOR OVERWEIGHT AND OBESITY IN CHILDREN AND ADOLESCENTS

ENDOCRINE FACTORS

The endocrine factors of obesity include: lack of growth hormone, hypothyroidism (lack of thyroid hormone) and Cushing's syndrome (excess secretion of cortisol). These factors lead to reduced growth rate and lower growth, while normal or accelerated growth rate excludes endocrine causes of obesity and mainly follows the genetic potential inherent in each individual. Acceleration of growth in children can be a consequence of Albright's hereditary osteodystrophy (pseudohypoparathyroidism type Ia) in the first two to three years, and after that age they are of lower growth. Hypothalamic obesity occurs as a result of damage to the hypothalamus by a tumor or surgery or radiotherapy. In children and adolescents, it is most often manifested by a normal growth rate, even though they have a lack of growth hormone, obesity and symptoms of tumor disease (11).

GENETIC FACTORS

Genetic factors have an impact on fat metabolism and control and regulate hormones that affect appetite. They are considered responsible for 30% to 70% of obesity cases. They affect the rate of metabolism, the way fat is distributed in the body, and the energetic reaction to excessive eating. The lack of the hormone leptin in the body leads to a constant state of hunger, which results in excessive food intake in the body and leads to the development of obesity and metabolic disorders such as insulin resistance and dyslipidemia (12,13). Its role is to send information to the body when it is hungry and when it is full. The discovery of more than 60 genetic markers responsible for increased susceptibility to obesity in an individual is certainly significant in terms of genetic research. The difference between individuals in BMI with a difference of 1.45% is associated with the 32 most common genetic variations. Thus, carriers with more than 38 different alleles have the highest risk for obesity and an average BMI higher by 2.7 kg/m² compared to those with low genetic risk. Although genetics plays an important role in the development of obesity, other risk factors such as diet, parental obesity, physical activity and sedentary lifestyle, endocrine disorders, smoking, socioeconomic factors, and general lifestyle should be taken into account (14).

NUTRITION

Proper nutrition is considered one of the most important factors that affect the development of the organism, the state of nutrition and contributes to the preservation of health. Children and adolescents are the most sensitive population to improper nutrition because the way they eat determines their emotional

and psychophysical development, affects school achievements and health in later life (15). Proper nutrition as well as proper eating habits during the growing up period of children are responsible for their physical, psychosocial and cognitive growth and development. As a consequence of bad eating habits from the aspect of increased energy intake, and correspondingly reduced energy consumption, obesity and comorbidities arise. To maintain the body's function and health, it is necessary to satisfy the body's needs for daily energy intake and a sufficient amount of protective and nutritional substances, which can only be achieved through proper nutrition. Nutrients are divided into micronutrients (vitamins and minerals) and macronutrients (proteins, carbohydrates and fats), and growth and development, especially during childhood and adolescence, require greater needs for nutrients, and the requirements for energy and nutrition should correspond to their needs. During growth and development, there are increased needs for minerals (calcium, zinc, iron), vitamins (B complex vitamins, vitamin C, vitamin D), and insufficient protein needs affect muscle development and energy level (16,17). In general, school children have irregular meals, most of them do not consume cooked food, nor do they have adequate representation of micronutrients, macronutrients and dietary fiber in their diet. The composition of the main meals is usually based on the consumption of red meat, potatoes and pasta, and they are very scarce with portions of fruits and vegetables. Also, unhealthy snacks such as high-calorie fruit juices, fatty crackers and an abundance of sweets, in addition to all of the above, contribute to the development of obesity, so an obese child most often grows into an obese person. With increasing age, it was observed that students have more irregular eating habits (irregular breakfast, more frequent consumption of sweets and snacks, reduced consumption of fruits and vegetables, increased intake of fast food and carbonated juices) (10). Increasing the intake of fast food can lead to a higher risk of overweight and obesity, especially in children and adolescents. These foods contain very high levels of calories, saturated fat, trans fat, sugar, sodium, and simple carbohydrates. It is very affordable because it is sold at very low prices (18). Poor and inadequate nutrition, combined with a decrease in physical activity and an increase in sedentary behavior, causes overweight and obesity in children and adolescents (19). There has been an increase in the size of portions as well as the consumption of high-energy foods, and a decrease in the intake of vegetables and fruits, which, in combination with physical inactivity, results in abdominal obesity and the development of cardiovascular diseases, neoplasms and metabolic diseases (20). In addition to adults, these problems affect children and adolescents all over the world. Adequate nutrition and physical activity in children with type 1 diabetes have a positive correlation with the course of the disease and treatment (20). That is why planning a proper (balanced) diet is very important for the proper growth and development of an individual or a certain population, because it aims to improve health and prevent the onset of diseases through defined energy values and nutritional structures (21). Many countries in the world, in order to prevent diseases that arise as a result of poor nutrition, introduce educational lectures in schools and teach children about healthy lifestyle habits (healthy diet, physical activity), which resulted in a positive development of knowledge about nutrition in children and changes in nutrition by consuming healthy food (22). Social networks (Internet), which are an integral part of children's environment and are often used as a learning tool, can serve as an effective method for providing additional information about good eating habits of children and adolescents (23). Table 1 shows "healthy foods" that are recommended in the diet of children and adolescents and "unhealthy foods" that should be avoided or consumed in minimal quantities. In addition to a good/correct selection of foods, it is necessary to consume a lot of liquid (water).

Table 1. Tabular representation of examples of “Healthy and unhealthy foods”

Healthy food	Unhealthy food
Bread, rice, flour, potatoes, pasta, cereals	“fast food”
Fruits/vegetables foods rich in vitamins, minerals, dietary fiber and antioxidants	All types of carbonated drinks Snacks
Dairy products (cheese, yogurt, milk), meat (fish), eggs rich in calcium, protein	low in saturated fat Oils, fats, concentrated sugars

PHYSICAL ACTIVITY

According to the results of scientific studies, children and adolescents in most countries have a low prevalence of overall levels of physical activity, a high prevalence of sedentary behavior and a growing prevalence of obesity, which can be associated with long-term risks for children’s health, including elevated levels of cholesterol, triglycerides and glucose in the blood (development of type 2 diabetes, high blood pressure). In adulthood, it is an important risk factor for the development of metabolic syndrome (19,24). Sedentary behavior is defined as time spent awake, sitting or lying down with low energy consumption in the context of educational, home and social environments and transportation. Includes: watching television, working on a computer, reading/studying while sitting, driving a car, using smartphones/tablets. Sedentary behavior in children and adolescents is associated with poor health outcomes and may lead to the development of obesity, which results in increased cardiovascular risk, type 2 diabetes, menstrual abnormalities, sleep-disordered breathing, or psychosocial effects (stigmatization of obese children) (25,26). It is recommended that children and adolescents limit the time they spend in a sedentary lifestyle, especially the time spent in front of screens, and to engage in various forms of physical recreation (27,28). The WHO guidelines regarding the physical activity of children and adolescents (5 - 17 years) from 2020 recommend that it be carried out as part of recreation and free time (games, sports or planned exercise), physical education, transportation (cycling, walking, wheelie driving), or performing household chores in the context of educational, home and community settings (29). In children and adolescents, physical activity has a positive effect on the cardiovascular profile, they are thinner and have better bone mineral density, which reduces the risk of developing osteoporosis in old age. Behavioral patterns are also transferred into adulthood, so active children remain physically active, which can be a prerequisite for good health (30). A generally active lifestyle and participation in daily physical activity that includes physical activity of light and moderate intensity in children and adolescents is recommended because it is associated with multiple positive health outcomes. The promotion of physical activity and its benefits for human health should be represented from the earliest childhood in all educational systems, recommended by teachers, parents and the wider social community.

ENVIRONMENTAL FACTORS

The emergence of obesity can also be observed in the context of complex social environments in which children and adolescents grow up. The mutual influence of these risk factors, such as family, peer groups, schools and communities, is reflected in the way of eating, physical activity and sedentary behavior. Parents represent the primary social context and pattern of behavior in the approach to nutrition and physical activity that children adopt and develop as healthy or unhealthy lifestyles (25). The role of parents is great in adopting healthy eating habits from an early age, because if parents adhere to them, children will accept them, especially if care is taken about main meals, snacks and healthier varieties of snacks. The results of longitudinal studies regarding children’s lifestyle (consumption of fast food, time spent in front of the screen, sports activities) show a stronger influence of their peers compared to the lifestyle of siblings

(25). Schools should also organize their own kitchens with the aim of promoting proper nutrition and applying it in practice (27). As children grow up and stay more and more outside the home environment, there are new social influences and a reduction in the influence of the family environment in eating habits. These changes are particularly visible during the transition from childhood to early adolescence, when the influence of peers increases and changes in eating behavior occur. Socializing with peers affects the change in the food environment, they buy more meals and snacks in fast food restaurants and reduce moderate to vigorous physical activity in combination with an increase in the time spent using smartphones and computers in their free time. Other studies have also shown that among adolescents, the intake of fast food and snacks, the level of physical activity and sedentary behavior in their free time correlates with their friends and peers (26,27). Thus, fast food restaurants (FFR) are considered environmental factors and are defined as places where unhealthy food is sold that has a negative impact on the environment (14).

SOCIOECONOMIC FACTORS

The emergence of obesity in early childhood is increasingly linked to poverty and poor nutrition, social stressors, lower parental education and lower income. These socioeconomic factors can affect the lower availability of high-quality food, and the consumption of energy-rich and nutrient-poor food. Also in economically developed countries with high incomes, obesity rates are higher in the lowest socioeconomic groups among children (1).

PSYCHOLOGICAL FACTORS

Obesity is a risk factor for depression in children and adolescents and vice versa. Adolescent girls with depression suffer from obesity much more often than adolescent boys (31). Also, due to excess weight, many adolescents have a lack of self-confidence, which leads to certain emotional problems and the most common symptoms of anxiety.

CONCLUSION

Obesity is a growing public health problem for both adults and children and adolescents. An obese child tends to be obese in adulthood. It is worrying that since the first recorded prevalence of obesity in 1975, we have a growing trend at the world level. Thus, in 2016, on a global level, it was estimated that 124 million children and adolescents aged 5-19 were obese, and 213 million of them were overweight. The reports of the World Health Organization state that 39 million children under the age of 5 are overweight or obese. Overweight and obesity are most often caused by several risk factors: improper diet, low level of physical activity and sedentary behavior in free time, endocrine and genetic factors. Also, the influence of environmental factors, certain socioeconomic factors can lead to the development of obesity, which in children and adolescents results in the appearance of certain psychological disorders. Therefore, the prevention of obesity is the most important, and measures should be started from early childhood through the implementation of intervention programs that would affect the risk factors of overweight and obesity, especially those that are variable such as physical activity and proper nutrition.

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Received: December 22, 2022

Accepted: March 15, 2023



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Acknowledgements

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