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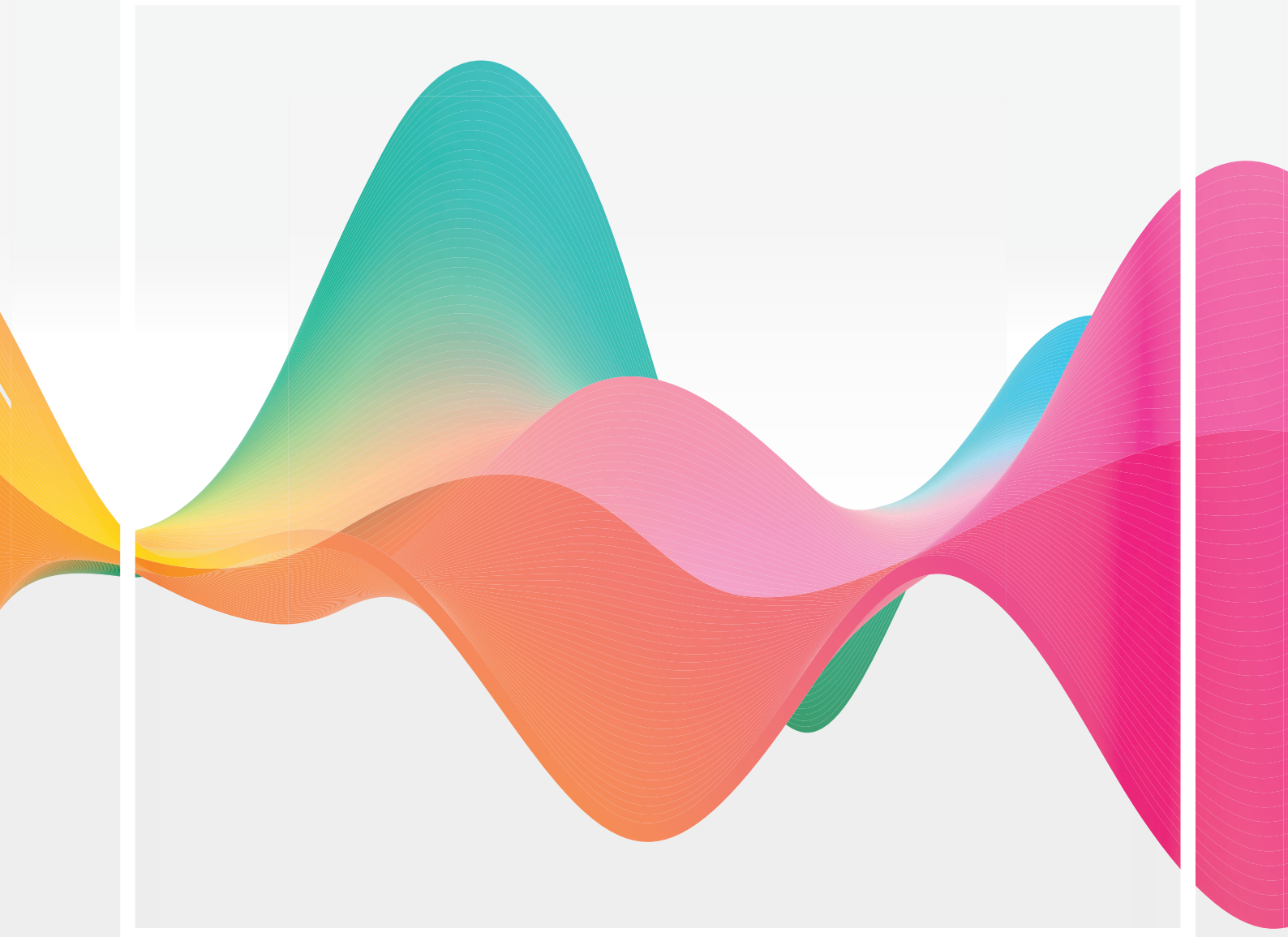
E-ISSN: 2791-6022
DOI: 10.26900/hsq

HEALTH SCIENCES QUARTERLY

International Peer-Reviewed and Open Access Electronic Journal

Formerly Name: JOURNAL OF SCIENTIFIC PERSPECTIVES
E-ISSN: 2587-3008



Volume: 1
Issue:2
2021

HEALTH SCIENCES QUARTERLY

E-ISSN: 2791-6022
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Formerly Name: Journal of Scientific Perspectives
E-ISSN: 2587-3008

International Peer-Reviewed and Open Access Electronic Journal

Volume 1
Issue: 2
July 2021

https://journals.gen.tr/jsp
hsq@holistence.com
Address: Sarıcaeli Köyü ÇOMÜ Sarıcaeli Yerleşkesi, Teknopark, No: 29, D.119
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ABOUT THE JOURNAL

About the Health Sci. Q.

Health Sciences Quarterly (Health Sci. Q.) journal as known by the name of "Journal of Scientific Perspectives" until April 2021 which has been published since 2017 is an international peer-reviewed journal of HOLISTENCE ACADEMY. It is published quarterly in January, April, July, and October. All manuscripts submitted for publication are evaluated by the editor-in-chief, section editor, editorial board, and referees. In addition, the journal provides a medium for highlighting selected articles reporting highly significant original findings, as Editor's Choice Manuscripts.

Aims and Scope

Health Sciences Quarterly (Health Sci. Q.) is an open-access journal that publishes original research papers, case reports, and reviews, clinical studies covering a wide range of subjects in life sciences and medicine as well as clinical and experimental investigations only in English.

Researchers in health sciences will find much of great use and interest in the Health Sci. Q..

HSQ aims to supply scientists of health with resources in order to provide the scientific knowledge through the publication of peer-reviewed, high quality, scientific papers and other material on all topics related to Medicine, Pharmacy and pharmaceutical sciences, Dentistry, Nursing, Bioethics, History of medicine, Health economics, Pharmacoeconomics, Medical education, Public health, and Epidemiology.

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EDITORIAL

Dear colleagues,

While the Covid-19 pandemic continues to affect all of the world, we are here with a new issue. Health Sciences Quarterly (HSQ) (formerly Journal of Scientific Perspectives) is an open-access journal that publishes original research papers, case reports, reviews, and clinical studies covering a wide range of subjects in life sciences and medicine as well as clinical and experimental investigations.

This issue includes four original articles and a review. We have carefully evaluated these articles, which we believe will contribute to the science and scientific community. We especially would like to thank the authors, the referees who reviewed the manuscripts carefully and everyone (also every life form) who contributed to these studies/articles.

Hope to meet in the upcoming issues with new studies.

Kind regards.

Hasan Erbay. MD, PhD, MBGPH
Editor-in-chief

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Volume : 1
Issue : 2
2021

E-ISSN: 2791-6022
https://journals.gen.tr/jsp

Received: 2021-05-29

Accepted: 2021-07-05

ORIGINAL ARTICLE

Relationship between depression and socio-demographic and illness characteristics in arsenicosis population of Bangladesh

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Abstract

A community based cross-sectional study was carried out by a self-structured questionnaire on 168 participants aged between 18 and 60 years at two arsenic prone area of Bangladesh to determine the association between extent of depression and socio-demographic as well as illness characteristics in arsenicosis population. The mean age ± SD was 42 ± 10.15 years. Female respondents were almost twice (63.1%) than the males (36.9%) in this study. Most of the respondents (94.0%) were shallow tube well water user. Among them most (80.0%) of the respondents were detected as arsenic contaminated water consumer over more than six months. Study estimated that almost half (44.3%) of the participants had suffered from mild to moderate depression in the moderate arsenicosis group. Less than quarter (20.8%) participants suffered severe depression in severe arsenicosis group. Quarter (26.7%) had mild arsenicosis with no depression. This difference was not significant. Gender had significant influence on proportion of level of depression. Females significantly suffered more from depressive symptoms than males. More than two third of the female respondents suffered from some kind of depressive symptoms; where less than one third of the males were suffered from depressive symptoms. Age has no significant relation with depression. Respondents who were 48 years and above age group had highest percentages of severe depressive symptoms (35.8%). This age group also suffered from highest percentage of mild to moderate depression (37.1%). Though most of the respondent (85.1) had no diabetes and hypertension. Respondents with physical illness suffered more from some sorts of depression than those without illness, but the result is not statistically significant. We understood that depression has health challenges in adult arsenicosis patients. Therefore, physicians should take account depression in their treatment management when deal with arsenicosis patients.

Keywords: *Depression, arsenic, arsenicosis, age, gender hypertension, diabetes, Bangladesh*

Citation: Islam MS, Akter F, Lasker SP. Relationship between depression and socio-demographic and illness characteristics in arsenicosis population of Bangladesh. Health Sci Q. 2021;2:53-61. https://doi.org/10.26900/hsq.1.2.01

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Introduction

Before 90s, rural population of Bangladesh used pond or small river as a means of drinking water and suffered from severe diarrhea due to bacterial contamination of surface water. The government with the help of international donor agencies (i.e., World Bank, United Nations Children's Fund) installed millions of shallow tube wells to provide groundwater in rural Bangladesh for safe drinking water. However, in 1993, it was discovered that these shallow tube wells are contaminated with geologically derived arsenic [1]. As a result, 50 million of people of 61 out of 64 districts of rural Bangladesh was exposed to inorganic arsenic (As) as a means of contaminating drinking water from these shallow tube wells [2]. Of 24 million people were suffered from severe form of arsenicosis that was the greatest disaster in the world [2]. Risk of arsenic poisoning in the population were increasing every day. Studies from US, Chile, Argentina, Mexico, Taiwan, Mongolia, West Bengal, India reported to health hazard of arsenic exposure from drinking water and most recently Bangladesh [2]. Over 100 million people in the world are suffered to As through drinking water. Chronic exposure to As in drinking water has been found relationships to many diseases, as for example skin cancer, lung, bladder, liver and kidney diseases, cardiovascular (ischemic heart disease, hypertension, stroke), endocrine (diabetes mellitus), hepatic, gastrointestinal, reproductive problems, cancer and neurodevelopmental (peripheral neuropathy, cognitive development) disorders [3-9]. Long time exposure through drinking arsenic-contaminated water affects all organs and systems of the body [8,9]. However, no report is available from arsenic toxicity on mental health specially depression and associated social consequences.

Depression is serious mood disorder causes negative feelings of self. The common symptoms of depression are loss of interest or pleasure, feelings of guilt or low self-esteem, no interest toward the external environment, tendency of suicide, sleep disorder (insomnia or spleen more), loss of appetite, and poor concentration. Chronic depression hamper to take care of everyday responsibilities by themselves [10]. According to World Health Organization (WHO), depression is the leading cause of disability as calculated by YLDs (Years Lost Due to Disability) and the 4th leading cause of the global burden of disease as measured by DALYs (Disability Adjusted Life Years) in 2000 [10]. If the forecast is true, by 2030, depression will be the second cause of the global disease burden.

Inadequate data are available on depression especially from arsenicosis patients in the general population in South Asia [10]. Bangladesh is not behind the scenario. Association of depression with arsenicosis in different cultural settings must be addressed. These facts had influenced us to examine depression among the arsenic endemic area. This study also estimated the extent of depression in arsenicosis population and relationship between depression of arsenicosis patients and socio-demographic characteristics of the respondents in Bangladesh. We assessed relationships of hypertension and diabetes with depression in arsenicosis patients as well.

Materials and Methods

A community based cross-sectional study was carried out by a self-structure questionnaire on 168 people at arsenic prone area of Nilkanda and Banglabazar village, Sonargaon, Narayanganj District of Bangladesh. Adult participants, age between 18 to 60 years were taken to determine the extent of depression in arsenicosis patients and socio-demographic and illness factors associated with it. Following socio-demographic factors were compared e.g., age, gender, education, marital status, family orientation and illness (hypertension and diabetes). Sample were taken purposively.

Ethical clearance was obtained from Sir Salimullah Medical College Ethical Review Committee. Consent was received from each individual prior to inclusion in the study. Participant had right to withdraw from the study at any stage. Confidentiality concerning their information were maintained strictly.

Self-structure questionnaire was developed in accordance with specific objectives. The questionnaire had 40 questions including: 1) socio-demographic characteristics, 2) illness characteristics, and 3) depression related information. Questionnaire was validated by a pre-test on 10 people in Monarbagh village under Sonargaon Upazia, Narayanganj district. Necessary modification was done according to their feedback and happy facial expression of participants with the questonaires. Data were collected through face-to-face interview. Study was elaborately explained to each prospective participant before the data collection start.

Depression status was assessed by Centre for Epidemiological Studies Depression (CES-D) scale. A Bangla version of CES-D was developed

according to Tsutsumi et al. to measure depression among arsenicosis patients of Bangladesh [11]. The CES-D score was used to understand mean of total depression score association with the discussing variables. Generally, cut-off value was used as 16 to identify respondents with clinically significant level of depression. Cut-off value were considered as <16 (no depression), 16-21 (mild to moderate depression) and ≥ 22 (severe depression) [12].

Arsenicosis was diagnosed from the record of Upazila Health Complex of Sonargaon Upazila, Narayanganj district. Documents of the respondents were reviewed for physical and psychological illness diagnosed by the physicians and Severity of arsenicosis were categorized according to WHO criteria.

The age of the respondents was divided into four groups with 10 years' interval. a) 18-27 years b) 28-37 years c) 38-47 years and d) 48 years and above.

After collection of all the information, data were checked, cleaned and edited. An analysis plan was developed according to objectives of the study. Data were analyzed using MS-Excel 2007, SPSS-16 version and Chi-square was done to compare level of arsenicosis and severity of depression. $P < 0.05$ was considered as statistically significant.

Results

Demography

The mean age ± Standart Deviation (SD) of respondents

Table 1. Demographic information (n=168)

Age group (yrs)	**n (%)**
18-27	14 (8.3)
28-37	42 (25.1)
38-47	56(33.3)
48 and above	56(33.3)
Sex of the respondents	
Male	62(36.9)
Female	106(63.1)
Marital status	
Married	136(81.0)
Unmarried	32(19.0)
Educational qualification	
Illiterate	60(35.8)
Primary	62(36.9)
Secondary	34(20.2)
Higher secondary and above	12(7.1)
Occupation	
Service holder	9(5.4)
Agricultural work	17(10.1)
Businessman	24(14.3)
Day laborer	19(11.3)
House wife	99(58.9)
Income level BDT	
<5000	55(32.7)
5000-10000	68(40.5)
≥10000	45(26.8)

Table 2. Sex of the respondents with severity of arsenicosis (n=168)

Gender		Severity of arsenicosis			χ^2	df	P
		Mild Arsenicosis n (%)	Moderate Arsenicosis n (%)	Severe Arsenicosis n (%)			
Gender of the respondents	Male	10 (16.1%)	33(53.2%)	19 (30.6%)	7.40	2	.240 n s
	Female	38 (35.8%)	42 (39.6%)	26 (24.5%)			

were 42 ±10.15 years & range between 21-60 years. Both age groups of 38-47 and 48 and above years had the highest portion of the respondents (33.3%) and quarter (25.0%) respondents had from age group of 28 to 37 years. Female respondents were almost twice (63.1%) than the males (36.9%). Most of the respondents (81%) were married. Education level of respondents were illiterate (35.8%), primary education (36.9%), secondary education (20.2%) and higher secondary and above (7.1%) respectively. More than half (58.9%) of the respondents were housewives followed by businessmen (14.3%) and service holder (5.4%). Forty percent respondents had monthly income between 5000-10000 taka. (Table 1).

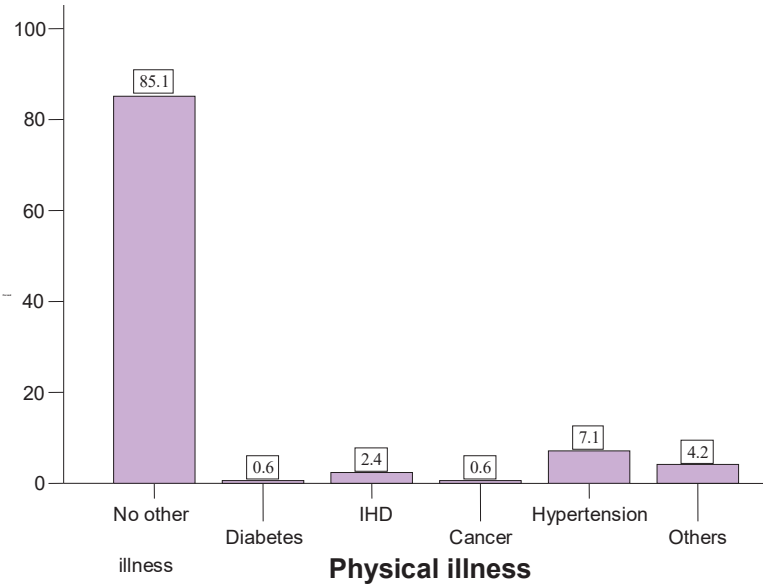

Figure 1. Distribution of respondents by physical illness

Source and duration of arsenic contaminated water

Most of the respondents (80.8%) used to consume arsenic contaminated water more than six months. Other had used tube deep well water.

Arsenic Patients

Females had suffered more arsenicosis than males. Among the study subjects (39.6%) female had developed moderate arsenicosis followed by severe arsenicosis (24.5%). In case of male, subjects (53.2%) had developed moderate arsenicosis and (30.6%) developed severe arsenicosis. But these differences were statistically not significant (p<0.240) (Table 2).

Physical illness

Most of the respondents (85.1%) were free from any sort of diagnosed physical illness and rest had physical illness (14.9%) like Hypertension, DM, and

Depression level

The Mean ≥ SD score of depression was 19.7 ≥ 7.90. Among the respondents, (71.4%) had suffered from some level of depression (CES-D score ≥ 16). About half of the study subjects (41.7%) suffered from mild to moderate depression followed by (31.5%) respondents had severe depression. No depression had (26.8%) cases (Figure-2).

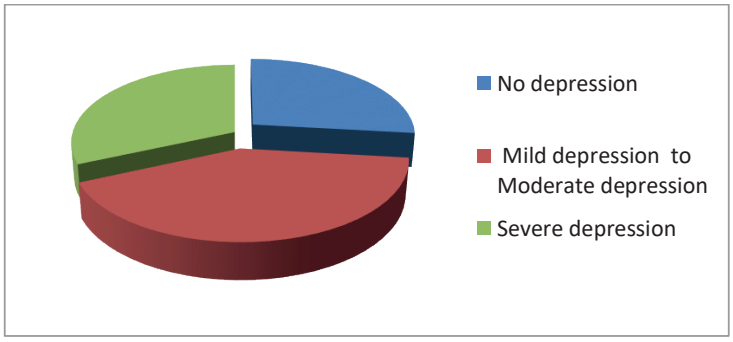

Figure 2. Level of depression among respondents

Table 3: Severity of arsenic with level of depression (n=168)

Depression level	Mild Arsenicosis n (%)	Moderate Arsenicosis n (%)	Severe Arsenicosis n (%)	χ^2	df	P value
No depression	12(26.7%)	20(44.4%)	13(28.9%)	1.86	4	0.760 ns
Mild to moderate depression	18(25.7%)	31(44.3%)	21(30.0%)			
Severe depression	18(34.0%)	24(45.3%)	11(20.8%)			

Table 4. Sex of the respondents and level of depression (n=168)

Characteristic	**Level of depression**			**Total n (%)**	χ^2	**df**	**p value**
Sex	No depression n (%)	Mild to Moderate depression n (%)	Severe depression n (%)				
Male	23(51.1)	20(28.6)	19(35.8)	62(36.9)	6.013	2	0.049*
Female	22(48.9)	50(71.4)	34(64.2)	106(63.1)			

Table 5. Age of the respondents and level of depression (n= 168)

Characteristic	**Level of depression**			χ^2	**df**	**p**
Age (in years)	No depression n(%)	Mild to Moderate depression n (%)	Severe depression n (%)			
18-27	8(17.8)	4(5.7)	2(3.8)	8.500	8	0.093 ns
28-37	12(26.7)	16(22.9)	14(26.4)			
38-47	14(31.1)	24(34.3)	18(34.0)			
48 and above	11(24.4)	26(37.1)	19(35.8)			

Severity of arsenic with level of depression

In mild to moderate arsenicosis group (44.3%) had suffered moderate depression In severe arsenicosis group had suffered severe form of depression and (26.7%) had mild arsenicosis had significantly no depression. This deference was not statistically significant (p>0.05) (Table 3).

Depression and Gender

Females were suffered significantly more from depressive symptoms than males. More than two third of the female respondents were suffered from depressive symptoms; whereas less than one third of the males were suffered from depressive symptoms. Females were suffering more from both mild to moderate and sever form of depression than males (mild to moderate 71.4% vs. 28.6% and severe form of depression 64.2% vs. 35.8%). Sex had significant influence on proportion and level of depression (p<0.05) (Table 4).

Depression and age

Respondents who were 48 and above year's age

Table 6. Physical illness and level of depression (n= 168)

Physical illness	Level of depression			Total	χ^2	*df*	*p*
	Mild Arsenicosis n(%)	Moderate Arsenicosis n(%)	Severe Arsenicosis n(%)				
No	42(29.4)	58 (40)	43 (30.1)	143 (85.1)	0.188	2	.188 ns
Yes	3(12.0)	12 (48.0)	10 (40.0)	25 (14.9)			

group had highest percentages of severe depressive symptoms 19(35.8%). This age group also suffered from highest percentage of mild to moderate depression 26(37.1%). However, Chi-square test could not find any significant relationship of depression level with age (p>0.05) (Table 5).

Depression and physical illness

Most of the respondents (85.1%) had no comorbidity like diabetes and hypertension. On the other hand, (14.9%) respondents had comorbid condition. But this finding was not statistically significant (p>0.05) (Table 6).

Discussion

Most of the respondents used shallow tube well water for drinking purpose (94%). This high percentage of use of shallow tube well was due to the location of study place which was an arsenic endemic area. Eighty percent of the respondents consumed arsenic contaminated water for more than six months and the rest 20% were both never user and less than six months. Why most of our study population still consume arsenic contaminated water where Government of Bangladesh install deep tube well for safe drinking water and painted red (3.5 million) for arsenic contaminated shallow tube well and green for deep tube well for non-contaminated tube wells to aware drinking safe tube wells water [13,14]. It might be the cause of most of the tube wells were installed privately [15]. So, poor people were not allowing to use these. Distance might be another cause of drink arsenic contaminated water. Previous shallow well is still in place. Moreover, installation shallow tube well was easy to draw up water by a hand pump drilling small diameter of pipe into. Therefore, families had no alternative but to drink from the contaminated well pire into the ground. [16].

Education

Percentage of depression score was found higher in low education group. Severe depression was higher among primary education group and mild to moderate depressive symptoms were more among illiterate respondents. But many studies showed that education can directly affect heath outcome by making process of information and health conscious [17,18]. Due to superstitions and prejudices of disease 30 to 80% people thought of arsenicosis as devil or impure air or a curse of God. All are them were uneducated and did not receive any treatment [19].

Gender

In our study more than 50% of the respondents were housewives. Work of house wife is non-paid occupation in our society, usually they were remaining at house doing house hold work and male counterpart went to work. Female had plenty of time to interview. This might be the cause of maximum female respondent of our study. Miyako et al. reported that there were the relationships between of unemployment and depression [20]. Moreover, female arcinocosis patients usually faced enormous social problems and social instability as well as marriage related problems [19]. However, in our study, we found that more than 70% of the housewives were suffered from all sorts of depressive symtoms which are consistent with previous report. In our study, females were suffered significantly more from depressive symptoms than males. Females were suffered more from both mild to moderate and severe form of depression than males (Table 4). Our study also revealed that moderate arsenicosis group 31 (44.3%) has suffered mild to moderate depression. Severe arsenicosis 11 (20.8%) had suffered severe form of depression. Before, 26.7% had mild arsenicosis had significantly no depression (Table 3).

Family status

In our society, most of the respondents had joint family. Female of joint family had higher depression score than nuclear family in the remote village. The people who were not drinking As contaminated water scared of arsenicosis, tend to avoid arsenic victims, barred from social activities, not allowed arsenicosis patients to attend social and religious programme, denied to take water from their deep tube well, not allowed to take baths in any of the village ponds/ river and students were debarred from school [10]. Social condition of married women of arsenicosis victim were grave, lead to a break-down of the marital relationships, some were separated or divorced or sent back to their parents' house [10,17]. Usually, people are not interested to make marital relationships with the families who were suffering from arsenicosis, that caused anxiety for both patients and parents of arsenic-affected area [17]. However, some studies conducted in arsenic affected areas reported that arsenic exposures are correlated with various neurologic problems [19]. In our study moderate arsenicosis group 31 (44.3%) has suffered mild to moderate depression. Severe arsenicosis 11(20.8%) had suffered severe form of depression. Though this deference were not statistically significant (Table 3).

Marital Status

In this study maximum respondents were married (81.0%). More than 70% severely depressed were married in arsenic patients in remote village in Bangladesh. Mild to moderate depression were also very much higher in married than not currently married. In our study shows that moderate arsenicosis group 31(44.3%) include in our study has suffered mild to moderate depression. Severe arsenicosis 11(20.8%) had suffered severe form of depression. A quarter had significantly no depression (Table 3).

Age

Our study could not detect statistically significant depressive symptoms in all age group. We found 48 years and above age group suffered from highest percentage of severe depression which is consistent with Valdes et al. They found that major depressive illness was associated with older age group [21]. Negative relation between age and depression was found U-shaped after adjusting for some sociodemographic factors [22].

Monthly income

Prevalent of arsenicosis patients were more among the poor [17] and had dietary deficiency [8]. They were remaining untreated due to financial constringent. Untreated poor victims are not capable of doing hard work and gradually lose strength. In Bangladesh lowest wage is BDTk 8000. In our space before in study, 40.5% had BDTk 5000-1000 income group and 32.7% were less them BTk 5000 and 26.8% more them BDTK 1000. In our study severe depression was found more among 5000 to1000 Tk monthly income group. Among the arsenicosis patient 40.8% had mild depression and severe depression patients were 35.0% followed by 24.2% had no depression.

Physical Illness

The different study showed association between depression with diabetes [23] or hypertension [24]. In our study, most of the respondents 143(85.1) had no space diabetes and hypertension. But respondents with physical illness suffered more from some sorts of depression than those without illness. But this finding was not statistically significant ($p>0.05$) (Table 6).

Arsenic and depression

Studies showed that that exposure to arsenic from drinking water was associated with reduced intellectual function [8,26]. Other study also found significantly association between arsenic-affected and poorer mental health [6,10]. A case-control study of Khan et al. in an arsenic-affected rural area in Bangladesh found significantly higher level of depression, weakness, restlessness, insufficient sleep, drowsiness and loss of appetite in case the group than [25]. They also reported include the after case that depressive feelings, fatigue and gastrointestinal symptoms which might be reflect of mental health problem in 61% of the cases group and around 44% of the controls group respectively [25].

Our study shows that moderate arsenicosis group 31(44.3%) has suffered mild to moderate depression. Severe arsenicosis 11(20.8%) had suffered severe form of depression. 26.7% had mild arsenicosis had significantly no depression. This deference was not statistically (Table 3).

Limitation

Our sample size was very small and was not representative of sample of the whole population. Depression was based on rather than a gold-standard diagnostic. Sampling technique was purposive to recruit the participant in the study due to time constraints. As a result, there might be some selection

bias. It may be evident to estimate the proportion of depression and factors associated with depression among arsenicosis patients.

Conclusion

Aim of this study was to assess the associated between extent of depression and different sociodemographic as well as illness factors in arsenicosis population. In our study moderate arsenicosis group 31 (44.3%) had suffered mild to moderate depression. Severe arsenicosis 11 (20.8%) had suffered severe form of depression. Though this deference were not statistically significant. Percentage of depression score was found higher in low education group. Severe depression was higher among primary education group and mild to moderate depressive symptoms were more among illiterate respondents. More than 70% of the housewives were suffered from all sorts of depressive symptoms in remote village of arsenic area. Gender had significant influence on proportion of level of depression. Females arsenic patients were more likely to suffer from both mild to moderate and severe depression than males. Age had no significant relation with depression. But respondents who were 48 years and above year's age group had highest percentages of severe depressive symptoms (35.8%). This age group also suffered from highest percentage of mild to moderate depression 37.1%. Family status, marrital status, income status had association with depressive symptoms. Most of the respondents had no diabetes and hypertension. But respondents with physical illness suffered more from some sorts of depression than those without illness. Arsenic exposed and patients with arsenicosis were found more likely to develop depressive symptoms.

Recommendation

During treatment planning process depression should be taken into an account in arsenicosis patients. Noncompliant arsenicosis patients should be routinely screened for depressive symptoms. Primary care physicians should be informed about the co morbidity of depression among arsenicosis patients.

Funding

We did not have financial support from any source for this study.

Conflict of interest

The authors declare no conflicts of interest.

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HEALTH SCIENCES QUARTERLY

Volume : 1
Issue : 2
2021

E-ISSN: 2791-6022
https://journals.gen.tr/jsp

Received: 2021-06-13

Accepted: 2021-06-25

ORIGINAL ARTICLE

Ganglion cell complex analysis in thalassemia major patients measured by optical coherence tomography

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Abstract

To analyze the changes in ganglion cell complex (GCC), peripapillary retinal nerve fiber layer (RNFL) thickness and central macular thickness (CMT) on spectral domain optical coherence tomography (OCT) in patients with thalassemia major. Forty one eyes of 41 patients with thalassemia major and 41 eyes of 41 healthy subjects were included in this prospective and comparative study. Peripapillary RNFL thickness, CMT and macular GCC thickness were evaluated with OCT (Cirrus HD-OCT 5000 Carl Zeiss Meditec, Inc, Dublin, CA, USA) in all patients and healthy controls. Additionally, disease duration, serum ferritin level, hemoglobin concentration, the dosage and duration of chelation therapy, count of transfusion, patient's weight were analyzed in thalassemia major group. RNFL thickness values were lower in the thalassemia patients but the difference was not statistically significant (except superior quadrant) and there was no significant differences in the mean CMT measurements. GCC thickness was thinner in all areas (average, superior, inferior, superior-temporal, inferior-temporal, superior-nasal, inferior-nasal) but only the thinning in the inferior-temporal was statistically significant. GCC and RNFL thickness changes occur earlier than CMT changes in β-thalassemia major patients. GCC thickness measurements can be used for follow-up in combination with other diagnostic methods.

Keywords: *Iron, thalassemia major, optical coherence tomography, ganglion cell complex, retinal nerve fiber layer*

Citation: Koca S, Yakarisik S. Ganglion cell complex analysis in thalassemia major patients measured by optical coherence tomography. Health Sci Q. 2021;2:63-68. https://doi.org/ 10.26900/hsq.1.2.02

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Introduction

Beta thalassemia (β- thalassemia) is one of the most common hereditary blood disorder characterized by genetic mutation and resulting in defective β-globin chain synthesis. It leads to hypochromic microctic anemia with erythrocyte displasia and destruction [1,2]. β- thalassemia major patients have severely diminished β- globin synthesis and requires regular red blood cell transfusions lifelong to survive. Regular transfusion regimen results with iron accumulation which leads to multiple organ failure. Iron chelator drugs are applied to diminish iron accumulation and prevent it's toxic effects [3,4]. Deferoxamine is the oldest iron chelator drug administered through subcutaneous injection. In recent years two forms of oral chelators (Deferasirox and Deferiprone) were introduced [5,6].

Thalassemia and it's management drugs can lead to various ocular problems such as retinal pigment epithelium degeneration, angioid streaks, venous tortuosity, visual field defects, deterioration of color vision, decreased visual acuity and optic neuropathy [7,8]. Iron deposition in ocular tissues and iron chelator treatments may play role in the pathogenesis of ocular involvement. Patients with β-thalassemia are mainly exposed to oxidative stress due to iron overload and antioxidants play an essential role in protection of the cells from oxidative damage [9].

Optical coherence tomography (OCT) can perform non-invasive in vivo evaluations have come into clinical use to evaluate the thickness of the peripapillary retinal nerve fiber layer (RNFL), ganglion cell complex (GCC), and choroid layer in various disorders [10]. High-resolution spectral domain-OCT techniques and computerized algorithms for image analysis have further improved the segmentation and measurement of specific retinal layers such as the GCC which is defined as the three innermost retinal layers: the nerve fiber layer, the ganglion cell layer, and the inner plexiform layer.

This study was conducted to assess the changes of macular GCC, peripapillary RNFL thickness and central macular thickness (CMT) in multi-transfused β-thalassemia major patients and compare with healty controls. Additionally, their relationship with disease duration, serum ferritin level, hemoglobin concentration, the dosage and duration of chelation therapy, count of transfusion, patient's weight were aimed to be studied.

Materials and Methods

Study population and design

This cross-sectional, comparative study was conducted between June 2020 and September 2020. The study was organized in accordance with the ethical standards and informed consent was obtained patients and their guardians.

We recruited a sample of 41 patients with β-thalassemia major and 41 randomly selected age-sex matched healty controls, aged between 13 and 48. Right eye of each patient was used for analysis. We excluded from the study patients with previous ocular trauma and ocular surgery, refractive error more than ±3 diopters, uveitis, glaucoma, retina and optic nerve diseases, any systemic diseases other than thalassemia and it's complications. Diabetes mellitus cases secondary to thalassemia were excluded from the study.

The diagnosis of β-thalassemia major was based on complete blood count, peripheral blood evaluation, hemoglobin electrophoresis and genetic mutation analysis of the patients. Serum hemoglobin concentration, ferritin level, the dosage and duration of chelation therapy, number of transfusion per year and patient's weight were recorded in β-thalassemia major patients.

All participants underwent a complete ophthalmologic examination including best corrected visual acuity (BCVA) using the decimal system, intraocular pressure (IOP) by air-puff tonometry, slit lamp biomicroscopy and dilated fundus examination, OCT measurements (peripapillary RNFL thickness, CMT and macular GCC thickness). Additionally disease duration, serum ferritin level, hemoglobin concentration, the dosage and duration of chelation therapy, count of transfusion, patient's weight were recorded in β-thalassemia major patients.

We obtained images after dilatation of pupil with Cirrus HD-OCT 5000 (Carl Zeiss Meditec, Inc, Dublin, CA, USA) by the same examiner. The Optic Disc Cube 200 × 200 protocol was used and average RNFL thickness and RNFL value by quadrants (superior, inferior, temporal and nasal) on a measurement circle 3.46 mm in diameter were calculated. The Macular Cube 512 × 128 protocol was used for the CMT and GCC thickness measurements. The Cirrus HD-OCT ganglion cell analysis algorithm was used to process the data. Images with movement artifacts, signal strength below 7/10, segmentation errors or poor centralization were rejected to ensure accurate results.

Statistical Analysis

Statistical analysis performed with IBM SPSS Statistics software ver. 25 (IBM Corp., Armonk, NY). Chi-square test was used to compare the categorical variables. Normality assumption of numerical variables was assessed with Shapiro Wilk test. Mann Whitney U test was used to compare non-normal distributed variables for two groups. Independent samples t test was used to compare normally distributed variables for two groups. Spearman Correlation Analaysis was used for relations between numerical variables. A p-value <0.05 was considered statistically significant.

Results

We evaluated a total of 41 patients with β-thalassemia major and 41 sex and age matched healty controls during the study period. Of the 41 patients, 22 (%53.7) were female and 19 (%46.3) were male in both groups. The mean age for the β-thalassemia major and control group were 24.34±8.58 years [range 13-48].

The values and comparisons of RNFL thickness in average and all four quadrants (superior, inferior temporal, nasal), CMT and GCC thickness (average, superior, inferior, superior-temporal, inferio-temporal, superior-nasal and inferio-nasal quadrants) are summarized in Table 1.

Although the average and all four quadrants RNFL thickness values were lower in the thalassemia group, the difference was not statistically significant, except superior quadrant (p=0.024 in superior quadrant). There was no significant differences in the mean CMT measurements. The GCC thickness was thinner in patients with β-thalassemia major in all areas (average, superior, inferior, superior-temporal, inferior-temporal, superior-nasal, inferior-nasal) but only the thinning in the inferior-temporal was statistically significant (p=0.025).

In β-thalassemia major group, the mean disease duration was 23.5± 8.6 years. The mean serum ferritin level and hemoglobin concentration were 1522.3±1777,8 ng/ml and 9.3±0.7 g/dL, respectively. Deferasirox was used in all thalassemia patients as chelation therapy. The mean dose and duration of chelation therapy were 1519,2± 529.9 mg and 21.3±9 years, respectively. The annual number of transfusions was 34.3±6 per year. Mean weight of thalassemia patients was 52.8± 11.6 kg.

The correlation between disease duration, serum ferritin level, hemoglobin concentration, the dosage and duration of chelation therapy, count of transfusion, patient's weight and OCT parameters are shown in Table 2 and 3. In correlation analyses, there was no statistically significant influence of disease duration, serum ferritin level, hemoglobin concentration, the dosage and duration of chelation therapy, count of transfusion, patient's weight for any RNFL thickness and CMT measurement in the β-thalassemia major group.

Although disease duration was negatively correlated with GCC thickness in all areas, it was statistically significant only in the average GCC thickness (p=0.045). There was a positive correlation between GCC thickness and the serum ferritin level (p=0.037 for inferior, p=0.025 for superior-nasal) and a negative correlation between GCC thickness and hemoglobin level (p=0.047 for superior, p=0.041 for inferior,

Table 1. The value and statistical comparison of OCT measurements.

	Thalassemia group	Control group	p
RNFL thickness (µm)			
Average	99.7 ± 7.8	100.9 ± 18.7	0.134
Superior	120.1 ± 13.9	128.2 ± 18.3	0.024
Inferior	133.8 ± 16.6	136.7 ± 18.9	0.463
Temporal	66.7 ± 7.7	69.1 ± 9.5	0.223
Nasal	77.3 ± 11.6	80.3 ± 17.2	0.357
CMT (µm)	244.2 ±18.2	244.6 ± 19	0.963
GCC thickness (µm)			
Average	83.1 ± 5.7	85.3 ± 4.6	0.055
Superior	84.1 ± 6.1	85.9 ± 5.5	0.170
Inferior	82.2 ± 6.4	83.9 ± 5.3	0.192
Superior-temporal	81.5 ± 5.8	83.1 ± 4.9	0.163
Inferior-temporal	82.2 ± 6.3	85.2 ± 5.6	0.025
Superior-nasal	84.7 ± 6	86.7 ± 5.3	0.061
Inferior-nasal	83.9 ± 5.9	85.8 ± 4.8	0.103

CMT: central macular thickness, GCC: ganglion cell complex, RNFL: retinal nerve fiber layer

Table 2. Correlation between disease duration, serum ferritin level, hemoglobin concentration, the dosage and duration of chelation therapy, count of transfusion, patient's weight and OCT parameters.

		Disease duration	Ferritin	Hemoglobin	Chelation duration	Chelation dose	Transfusion count/ year	Patient's weight
RNFL thickness								
Average	r	-0.086	-0.074	-0.167	-0.188	-0.144	0.034	0.070
	p	0.591	0.646	0.297	0.238	0.383	0.831	0.664
Superior	r	-0.046	0.041	-0.145	-0.138	-0.056	0.011	0.111
	p	0.774	0.799	0.367	0.390	0.737	0.946	0.491
Inferior	r	-0.085	0.105	-0.258	-0.223	-0.053	0.129	0.205
	p	0.599	0.513	0.104	0.161	0.747	0.421	0.198
Temporal	r	-0.101	0.237	0.075	-0.112	0.116	-0.121	0.058
	p	0.532	0.136	0.642	0.488	0.484	0.450	0.719
Nasal	r	-0.149	-0.170	-0.223	-0.164	-0.284	0.019	-0.035
	p	0.352	0.287	0.161	0.304	0.080	0.906	0.827
CMT	r	-0.112	0.036	0.022	-0.146	-0.026	-0.241	-0.016
	p	0.487	0.823	0.889	0.364	0.874	0.128	0.919

CMT: central macular thickness, RNFL: retinal nerve fiber layer

Table 3. Correlation between disease duration, serum ferritin level, hemoglobin concentration, the dosage and duration of chelation therapy, count of transfusion, patient's weight and GCC thickness.

		Disease duration	Ferritin	Hemoglobin	Chelation duration	Chelation dose	Transfusion count/ year	Patient's weight
Average	r	-0.314	0.293	-0.291	-0.287	0.052	0.071	-0.077
	p	0.045	0.063	0.065	0.069	0.752	0.658	0.634
Superior	r	-0.284	0.304	-0.312	-0.256	0.058	0.094	-0.034
	p	0.072	0.053	0.047	0.107	0.724	0.560	0.835
Inferior	r	-0.278	0.328	-0.321	-0.265	0.102	0.037	-0.060
	p	0.078	0.037	0.041	0.094	0.535	0.819	0.708
Superior-temporal	r	-0.223	0.144	-0.374	-0.167	0.076	0.074	-0.060
	p	0.161	0.371	0.016	0.298	0.647	0.644	0.708
Inferior-temporal	r	-0.233	0.232	-0.306	-0.184	0.040	0.044	-0.005
	p	0.143	0.144	0.052	0.249	0.808	0.785	0.974
Superior-nasal	r	-0.253	0.349	-0.233	-0.225	0.101	0.157	-0.046
	p	0.110	0.025	0.143	0.157	0.540	0.327	0.775
Inferior-nasal	r	-0.316	0.287	-0.263	-0.328	0.013	0.101	-0.126
	p	0.044	0.068	0.097	0.036	0.939	0.531	0.431

p=0.016 for superior-temporal). No significant correlation was found between GCC thickness and chelation therapy duration, except inferior-nasal area (p=0.036). Chelation therapy dose, transfusion count and patient's weight were not correlated with GCC thickness.

Discussion

Although the mechanism is not fully understood, β-thalassemia major patients represent various ocular manifestations. In previous studies, pathological findings including retinal pigment epithelium degeneration, angioid streaks, venous tortuosity, visual field defects, deterioration of color vision, decreased visual acuity, optic neuropathy, thicker lens and cataract have been reported in β-thalassemia major patients [4,7,8,11].

Iron is essential for many metabolic processes but excess iron can be toxic to tissues. In retina, iron is particularly critical for the visual phototransduction cascade for isomerohydrolase activity and catalyzing the conversion of hydrogen peroxide to hydroxyl radical which is the most damaging of the reactive oxygen species. Excessive generation of free

radicals can cause oxidative damage to biological macromolecules such as DNA, lipids, carbohydrates and proteins. Increased intraocular iron has been shown to cause oxidative injury to the retina [12-14]. Manafikhi et al. reported that thalassemic patients had lower total antioxidant capacity compared to healthy subjects and there was no relationship to disease severity [14].

Iron overload is unavoidable in thalassemia patients due to life-long transfusions. Iron- chelating drugs are used to prevent transfusion related complications. Deferoxamine has well-documented ocular side effects including retinal changes ranges from peripheral pigmentary changes to bulls-eye maculopathy [15,16]. Deferasirox is a new iron chelator drug that have been introduced as an orally effective alternative for deferoxamine. There are studies showing that it may be toxic to the eye although it's side effects are less compared to Deferoxamine. In a recent study, ERG and mfERG responses were reduced in thalassemic patients regardless of the type of chelation therapy they received [17]. On the contrary Sakamoto et al. suggested that iron-chelating agents was protected retinal neurons against excitoneurotoxicity via reduction of iron content and oxidative stress in the rats [18]. The toxic effects of iron chelation therapy on the retina and its mechanism were not fully understood.

We speculate that iron accumulation in retinal tissues, increased oxidative stress and decreased antioxidant capacity may lead damage to retinal structures and accelerate ganglion cell injury in β-thalassemia major patients.

In the current study, we found that RNFL thickness values were lower in the thalassemia patients but the difference was not statistically significant (except superior quadrant) and there was no significant differences in the mean CMT measurements. As in our study, Acer et al. found retinal nerve fiber layer thickness and subfoveal choroidal thickness was not statistically significant different in children with thalassemia minör [19]. Aksoy et al. reported that peripapillary RNFL was thinner in tha-major in all quadrants and thinning of the RNLF was correlated with hemoglobin value and ferritin level, but not with number of transfusions and visual acuity [20]. In β -thalassemia major patients Uzun et al. also observed that RNFL was thinner in all quadrants than control subjects and thinning was not correlate with hemoglobin or ferritin levels [21]. According to our study neither average and four quadrants RNFL thickness nor CMT were correlated with the disease duration, serum ferritin level, hemoglobin concentration, the dosage and duration of chelation therapy, count of transfusion, patient's weight.

Although the RNFL thickness and CMT has been investigated widely, GCC thickness changes in β-thalassemia major patients have been evaluated less. In our study we found the GCC thickness was thinner in patients with β-thalassemia major in all areas (average, superior, inferior, superior-temporal, inferior-temporal, superior-nasal, inferior-nasal) but only the thinning in the inferior-temporal was statistically significant. In correlation analyses, disease duration was negatively correlated with GCC thickness in all areas, it was statistically significant only in the average GCC thickness. Also hemoglobin level was negatively correlated with GCC thickness in superior, inferior, and superior-temporal area. There was a positive correlation between GCC thickness and the serum ferritin level in inferior and superior-nasal areas. No significant correlation was found between GCC thickness and chelation therapy duration (except inferior-nasal area), Chelation therapy dose, transfusion count and patient's weight. In β -thalassemia major patients Ulusoy et al. observed that peripapillary RNFL thickness in all quadrants, CMT and macular average GCC were thinner but there were no statistically difference. They also reported that RNFL, CMT, and GCC thicknesses were not correlated with hemoglobin, hematocrite, ferritin, and other demographic characteristics [22]. Our study showed that GCC thickness changes occur earlier than RNFL and CMT changes in β-thalassemia major patients. GCC thickness can be used for earlier diagnosis and follow-up in combination with other diagnostic methods. The limitations of this study was the relatively small number of cases.

Conclusion

Since life expectancy in thalassemia major patients has improved over time, the risk of ocular abnormalities due to diease and drugs used in treatment increases. Therefore, regular long-term follow-up of these patients has become more important to prevent further sight-threatening ocular complications. GCC thickness can be used for earlier diagnosis and follow-up along with other imaging methods.

Funding
The authors declared that this study has received no financial support.

Conflict of interest
The authors have no conflicts of interest declared.

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HEALTH SCIENCES QUARTERLY

Volume : 1
Issue : 2
2021

E-ISSN: 2791-6022
https://journals.gen.tr/jsp

Received: 2021-05-25

Accepted: 2021-06-11

ORIGINAL ARTICLE

Epidemiologic and clinical evaluation of the acute intoxication in pediatric patients

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Abstract

Acute poisoning is a critical and emergent public health problem worldwide among pediatric age group. The common epidemiological observation is required to understand the characteristics of the pediatric intoxication for each location and important for management the poisoning cases. This retrospective study researched the epidemiology of poisoning among children. This study represented the epidemiology of poisonings of children admitted to the pediatric intensive care unit at Afyonkarahisar Health Science University Faculty of Medicine between February 2020 and May 2021. Fifty one pediatric patients were reffered to the PICU due to acute intoxication. 58.9% of the analyzed patients were male and 41.1% were female. The mean age of all patients was 8.57±7.6. The majority of cases were due to drug-related poisonings. The average age of cases of suicidal poisoning was higher than accidental intoxication cases. Paracetamol was the most prevalent cause of drug-related intoxication and more common in children under 5 years of age and selective serotonin reuptake inhibitors were more frequent in adolescent group. All patients survived. Almost all of the patients were discharged from hospital within 3 days. Poisonings are still a serious reason for morbidity and mortality in developing countries among children. Early awareness of poisoning and appropriate management appeared to be effective and to decrease the mortality rate.

Keywords: *Poisoning, intensive care unit, pediatric, management*

Citation: Celegen M, Celegen K. Epidemiologic and clinical evaluation of the acute intoxication in pediatric patients. Health Sci Q. 2021;2:69-73.
https://doi.org/ 10.26900/hsq.1.2.03

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Introduction

Acute intoxication is a prevalent and significant fatal public health problem in children despite regulatory intervention and medical advances and also represents a frequent reason of admission in emergency departments, which contributes to additional costs of patient care [1]. Although poisoning may occur at any age, the incidence of childhood poisoning is most commonly observed at children younger than six years of age [2]. The cause of poisoning varies with age, gender, education, and cultural background, and also shows seasonal variations. House cleaning products poisoning is most common cause of intoxication agent at 3-5 years of age, drugs used for committing suicide are the primary cause of intoxication at school age groups [3]. Poisoning exposure usually causes minor symptoms or commonly asymptomatic on admission in young children; the mortality rate of poisoning is approximately 3-5% [3]. Epidemiological documentation of childhood poisonings for each region is very important for prevention and understanding of characteristics problem of poisoning and also these information contribute the development of health policies and treatment plans. In this article, we investigated the pediatric patients who were hospitalized because of acute poisonings in the pediatric intensive care unit (PICU). The main aim of this research was to present the epidemiology, pattern, duration and the outcome of management of poisoned patients.

Materials and Methods

The data of all patients aged 0-18 years who were hospitalized to the pediatric intensive care unit at Afyonkarahisar Health Sciences University Faculty of Medicine for acute poisoning between February 2020 and May 2021 were investigated systematically in this retrospective clinical study. The diagnosis of poisoning was based on the history taken from the patient or their relatives. Acute food poisoning patients were excluded. Age and sex of patients, time from poisoning to arrival at the emergency department, symptoms and signs on admission, substances responsible from intoxication, the way of intoxication (accidental or suicide), specific and supportive therapies performed in the emergency department or pediatric intensive care unit, length of stay in the PICU, and the outcomes were noted. The computerized automation system of the university hospital was used to obtain of the data.

Ethical statement

The study protocol was approved by Afyonkarahisar Health Sciences University Medical Faculty Ethical Committee. All patient information was protected and kept confidential.

Statistical analysis

In statistical evaluation, SPSS 22.0 Windows program was used. Independent samples t-test or Mann-Whitney U test was used for comparison of continuous variables and Fisher's exact test or chi-square test for categorical variables. A p value less than 0.05 was accepted statistically significant.

Results

A total of 51 acute childhood poisoning cases were admitted to the pediatric intensive care unit of our hospital between February 2020 and May 2021. The mean age of all patients was 8.57±7.6. Thirty-one (58.9%) of them were male. Twenty six children, forming 51% of all patients, were under the age of five. Suicidal poisonings were significantly common in the female patients ($p < 0.001$). 41.2% of all patients were over 10 years old (n: 21 patients). According to age groups, 55% of patients older than 10 years of age were females. The average age of cases of suicidal poisoning was older than accidental intoxication patients (15.3 years vs. 4.08 years; $p<0.001$). The mean age of the cases presenting with suicide intoxication was 13.6 years.

Drug poisonings were the cause of poisoning in 86.2% of patients, although non-drug poisoning was encountered in 13.8% of patients. There was no significant difference in drug and non-drug intoxications by gender. Most of the cases (64.8%) were accidental poisoning. Thirteen poisoning cases occurred as a suicide attempt and 72.2% (n = 18) of these patients were girls. Twenty four children, forming 47% of all patients, were under five years of age and all these patients had accidental intoxication. 39.2% of all patients were older than the 10 years of age (n: 20) and 75% of these age group had suicidal intoxication (Table 1). Although poisoning occurred mostly in spring and winter months, there was no significant difference in overall seasonal distribution (Figure 1). While only 33.3% of patients referred to the emergency department within 60 minutes after initial poisoning incident, 68.7% referred within 2 hours, and 94.1% after 6 hours. The mean admission duration to the emergency department is 2.41 hours. Most cases of poisoning occurred at home 86.2% and

Table 1: Type of poisoning according to age groups

Age Groups	Suicidal n (%)	Accidental n (%)	Total
0-5	0	26 (78)	26 (51)
5-10	0	4 (12.1)	4 (7.8)
>10	18 (100)	3 (9.1)	21 (41.2)
Total	18 (100)	33 (100)	51 (100)

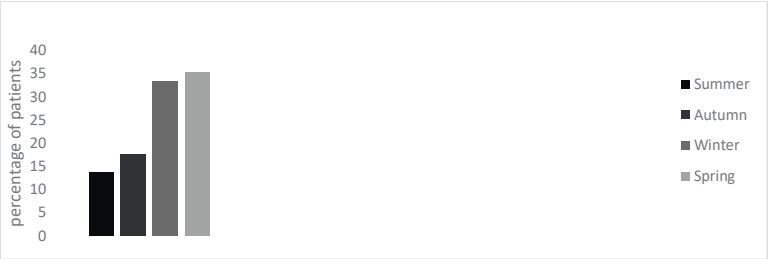

Figure 1. Seasonal distribution of poisoning cases

all intoxications were administered orally.

Drugs were the most common agents causing poisoning (84.3%) (Table 2). Paracetamol was the most prevalent cause of drug-related intoxication and more common in children under 5 years old. Selective serotonin reuptake inhibitors (SSRI) were the most common drug that causes poisoning older than 10 years of age and also among the cases of suicidal poisoning, SSRI were the most commonly ingested medication.

Gastrointestinal symptoms, nausea and vomiting, were the major complaint of patients at the admission to emergency department (38.8%), followed by neurologic symptoms like unconsciousness (%16.6).

In most cases management strategy was non-specific, including decontamination and supportive-symptomatic therapy. Gastric lavage was employed in 17 children and activated coal applied in 19 patients

Table 2. Agents causing poisoning

Agents	n (%)
Drugs	44
Alcohol	2
Corrosive Substances	3
Hydrocarbons	1
Insecticides	1

Table 3. Intensive Care Interventions for the Treatment of Intoxication

Interventions	n (%)
Gastric lavage	17(33.3)
Activated coal	19 (37.2)
Antidote	15 (29.4)
Alkalization	1(1.9)
Hemodialysis	2 (3.9)
Ventilatory support	1 (1.9)

who had ingested poison.

Esophagoscopy was performed only in 3 patients to evaluate the esophageal stricture who had ingested corrosive substances. Hemodialysis was performed in two patients who developed acidosis after alcohol intoxication. Mechanical ventilator support was applied to a patient with mefenamic acid intoxication due to respiratory failure. Alkaline therapy was administered to a patient with anticholinergic intoxication due to wide QRS tachycardia. N-acetyl cysteine was administered as an antidote to all patients with a history of toxic dose intake of paracetamol, although the blood drug level could not measure for technical reasons (Table 3). Fourty-four cases were discharged from health institution within 3 days. Seven cases hospitalized in PICU more than 3 days. Our patient's mortality rate was zero a result of poisoning.

Discussion

Acute poisoning is a well-known common problem in childhood period. Early and efficient intervention can reduces morbidity and mortality ratio. Recognition and documentation of epidemiological outlook and different factors for childhood intoxication is crucial for determining treatment choices and planning suitable preventive measures [4]. Epidemiological studies conducted for poisonings of all regions will provide better treatment for intoxication cases. Little information has been published concerning with childhood poisoning in our region. According to the World Health Organization (WHO), acute intoxication accounts for an estimated 45,000 deaths annually among pediatric age group and patients under the age of 20 years [5]. In Turkey poisoning range was between 0.21% and 6.2% [3].

In this study poisoning occurs more commonly in boys during the first five years of life and all of the cases were accidental poisoning. In older than 10 years age group, poisoning is more common in girls, usually involving suicidal intoxication type. Our findings of age group consistent with findings of previous studies. Ozdemir et al presented that poisoning were more frequent in males with younger than 5 years of age while in adolescent poisoning was more common seen in females [1]. Similar findings have been

reported from Sahin et al, male/female ratio was 1.06 in younger age patients and female predominance was present after ten years of age group [6]. Similar outcome have been reported several studies from Turkey and other developed countries [7-9].

Approximately eighty percent of our cases had been poisoned by drug-related agents. The same findings was reported in studies from developed and developing countries [1,6]. H Ozdogan et al presented that nearly two-third of their patients had been poisoned by other than pharmacological agents like foods, hydrocarbons, and pesticides [9]. Paracetamol was the first important cause of drug-related poisoning and more common among children under 5 years of age. Paracetamol and antidepressants were the most common causative agents of drug-related poisoning in the 1–4 age group in the study of Andiran et al [8]. Sertraline is one of the most frequently treatment modalities used in major depression, was the most common identified drug related poisonings older than 10 years of age in our study group. This was because of the antidepressant drugs were the medication of our patients so easy to access to agents. Tricyclic antidepressants were reported the most common intoxication agents in school-age children by Sahin et al [6]. The most s spectacular results in Ozdemir et al study were the increasing ratio of amitriptyline intoxication, while decreasing ratio of salicylate intoxication and rising count of suicide attempts in pediatric age group over the 33 years [1]. Similar result was reached in a study made by Gunnell, in that study one of the most commonly identified drug was antidepressants [10].

In our study we found that incidents of poisoning occurred more frequently in winter and spring.Similar findings was reported from another study that most poisonings occurred in spring months [6]. Accidental intoxication happened more common in summer and less frequently during the winter season. In other words, intentional intoxications peaked in winter months, although occurring less commonly during the summer in Turkey [1].

The clinical presentation of poisoning is different and nonspecific. Usually, gastrointestinal and neurological symptoms were seen in our study, which was associated to the frequency of intoxications from ingesting drugs.

In most cases, non-specific therapy was applied, including decontamination and supportive treatment. Gastric lavage was applied in 17 (33.3%) patients, and activated coal was given to 19 (37.2%) patients who came to emergency department within the first two hours following poisoning. Gastric lavage should be considered only within the first 60 minutes of ingestion and not performed routinely due to the associated with a 3% complication rate (12, 13).

In developed countries, average mortality rate is 1% as a result of acute poisoning, 3-5% in developing countries. In our study, none of our patients died (11). Our good prognosis in pediatric intoxication patients might be assignable to the fact that the more than half of poisoning patients involved accidental intoxications and visited emergency unit within 2 to 6 hours after poisoning.

Conclusion, most poisonings occurred in under five years old children via the accidental ingestion and drug-related ingestion was the leading cause of poisoning. Female adolescents' ratio were common among older age group. The result of this study facilitates especially paediatrician who work in Afyonkarahisar region to develop preparations for pediatric poisoning cases.

Study Limitations

There are three main limitations to our study. It was a single center retrospective study and conducted with a limited number of patients and almost all of our patients with mild clinical course.

Funding

This observational study not received any external funding.

Conflicts of Interest

All authors declare no conflict of interest relevant to this study.

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HEALTH SCIENCES QUARTERLY

Volume : 1
Issue : 2
2021

E-ISSN: 2791-6022
https://journals.gen.tr/jsp

Received: 2021-05-21

Accepted: 2021-06-09

ORIGINAL ARTICLE

An evaluation of quantitative body composition on thoracic computed tomography and the effect on clinical severity in patients with chronic obstructive pulmonary disease

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Abstract

The aim of this study was to evaluate the effect on disease severity of the quantitative measurements of pectoral muscle area (PMA), pectoral muscle index (PMI), pectoral muscle density (PMD), subcutaneous adipose tissue (SAT) and mediastinal adipose tissue (MAT) taken on thoracic computed tomography (CT) of patients with chronic obstructive pulmonary disease (COPD), according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification. A retrospective screening was made of patients diagnosed with COPD and applied with thoracic CT and respiratory function tests. A record was made of height, weight, body mass index, and smoking history (packet/year). On thoracic axial CT images, the PMA, PMI, PMD, SAT, and MAT values at the aortic arch level were calculated quantitatively using OsiriX software (Pixmeo, Switzerland). The patients were grouped as A-B-C-D according to the GOLD 2018 guidelines. Then two groups were formed as mild-moderate COPD (GOLD A-B) and severe COPD (GOLD C-D). The relationship was evaluated between clinical severity and quantitative body composition values according to the GOLD classification. A total of 80 patients diagnosed with COPD were included in the study comprising 61 males and 19 females. The GOLD A-B group included 43 (53.75%) patients and the GOLD C-D group, 37 (46.25%) patients. No significant difference was determined between the two groups in respect of the PMA, PMI, and PMD values (p=0.001). A statistically significant difference was determined between the groups in respect of the SAT and MAT values (p=0.001, p=0.002, respectively). A cutoff value of <30.04 in PMD (0.964; 95%CI:0.928-1) showed the best performance in predicting the mild-moderate COPD patients (GOLD A-B) with 92% sensitivity and 93% specificity. The results of this study demonstrated that PMD showed the best quantitative body composition performance in the differentiation of mild-moderate and severe COPD disease.

Keywords: *Body composition, chronic obstructive pulmonary disease, quantitative analysis, thoracic computed tomography*

Citation: Kaya F, Ozgul E, Balci A, Bozkurt E, Atay E. An evaluation of quantitative body composition on thoracic computed tomography and the effect on clinical severity in patients with chronic obstructive pulmonary disease. Health Sci Q. 2021;2:75-81. https://doi.org/ 10.26900/hsq.1.2.04

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Introduction

Due to the heterogeneity of chronic obstructive pulmonary disease (COPD), there is a need for more descriptive biomarkers in diagnosis beyond pulmonary function tests [1]. Thoracic computed tomography (CT) has been used for many years for the visual diagnosis of emphysema and to obtain a precise evaluation of the presence of COPD [2]. It is thought that body composition, which may vary in COPD patients, is a marker of the clinical process of the disease. In this context, body mass index (BMI) is related to the increased mortality rate in COPD patients. It is known that in previous studies, lean muscle mass has been preferred to BMI in COPD patients [3-5]. There is also known to be clinical importance of different body components other than lean muscle mass and BMI. Skin fold thickness, bio-impedance, and dual-energy x-ray absorbancy are other methods used to determin body composition. Previous studies have suggested that CT measurements could provide additional information about the body composition of patients who smoke [6,7]. Evaluation of the cross-sectional area of the mid-thigh muscle has been shown to be a stronger predictor of mortality in COPD than BMI [6]. Quantitative body composition values such as pectoral muscle area (PMA), pectoral muscle index (PMI), pectoral muscle density (PMD), subcutaneous adipose tissue (SAT) and mediastinal adipose tissue (MAT) have been examined on thoracic CT images in COPD and several pulmonary diseases [8-13]. In previous studies, muscle mass has been reported to be significantly reduced in COPD patients and has shown a correlation with disease severity [10,11]. The aim of this study was to evaluate the relationship of the body composition values of PMA, PMI, PMD, SAT, and MAT, measured quantitatively on thoracic CT, with disease severity according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification of COPD patients.

Materials and Methods

Patients diagnosed with COPD and applied with thoracic CT and respiratory function tests within the last year were identified from a retrospective screening of the hospital records system. Patients were excluded if there was an interval of more than one month between COPD diagnosis and respiratory function tests and CT scans, or if they had a known malignancy. A total of 80 COPD patients with non-contrast thoracic CT taken within the last year were included in the study. A record was made for each patient of height, weight, body mass index, and smoking status (packet/year).

Computed Tomography Technique

The images were acquired without contrast on a Toshiba Aquilion Prime (80x2) multi-slice CT device (Toshiba Medical Systems, Japan). After topogram acquisition, non-contrast images were taken during deep inspirium on two consecutive slices from the apexes as far as the bilateral adrenal glands, using tube voltage 120 kV, collimation 05x80 mm, image area 370mm, matrix 512 x 512, rotation speed 0.35 secs, table level 15 mm/sec, pitch factor 0.813 and helical pitch 65.0. The scanning time was 2-4 seconds.

GOLD Classification

Patients with post-bronchodilator FEV1/FVC<70% were accepted as having airway obstruction and were grouped as A-B-C-D according to the GOLD 2018 guidelines. In this classification system, GOLD A is defined as patients with low risk, few symptoms, 0-1 flare-ups, and mMRC grade 0-1 or CAT score <10, GOLD B as patients with low risk, more symptoms, 0-1 flare-ups, and mMRC grade ≥2 or CAT score ≥10, GOLD C as patients with high risk, few symptoms, ≥2 flare-ups, and mMRC grade 0-1 or CAT score <10, and GOLD D as patients with high risk, more symptoms, ≥2 flare-ups, and mMRC grade ≥2 or CAT score ≥10. For the evaluations in this study, two groups of patients were formed as mild-moderate (GOLD A-B) and severe (GOLD C-D).

Quantitative Computed Tomography Analysis

From a single axial slice thoracic CT image taken immediately over the aortic arch, measurements were taken of PMA, PMI, and PMD, and at the pectoral muscle level, measurements of SAT and mediastinal adipose tissue with OsiriX software (Pixmeo, Switzerland) in each patient (Figure 1). PMA was measured with threshold values of -50 to 90 Hounsfield Units (HU) [8,12], and SAT and MAT

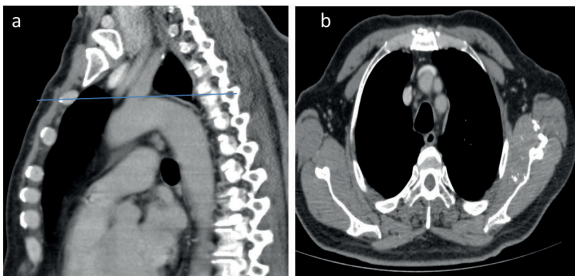

Figure 1. Determination of the cross-sectional area where quantitative body composition measurements were to be taken from the level of the aortic arch. (Blue line)

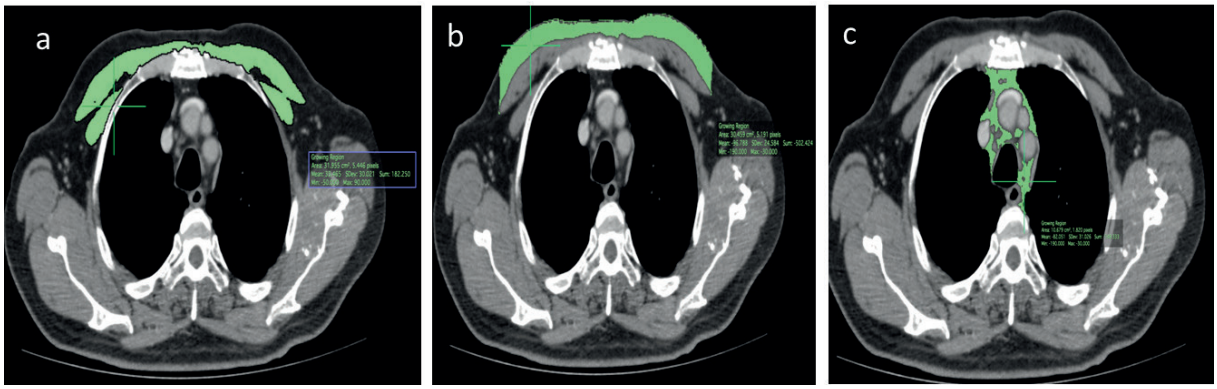

Figure 2. Measurement of PMA and SAT and MAT values from the same level

with threshold values of 190 to -30 HU (10). PMI (cm^2/m^2) was obtained as the ratio of height squared (m^2) to muscle area (cm^2) (Figure 2).

Statistical Analysis

Data obtained in the study were analyzed statistically using SPSS 25 software. Conformity of the data to normal distribution was assessed with histogram analysis and the Kolmogorov-Smirnov test. Variables showing normal distribution were analyzed with parametric tests, and those not showing normal distribution with non-parametric tests. In the analysis of differences between categorical variables, the Chi-square test was applied, and comparisons of variables between groups were made using the Student's t-test, the Mann Whitney U-test, and the Kruskal-Wallis test. ROC analysis was applied to determine the cut-off values for successful subtraction models and determine these values' sensitivity and specificity. Results were stated in a 95% confidence interval and a value of $p<0.05$ was accepted as statistically significant.

Results

The evaluation was made of a total of 80 COPD patients, comprising 61 males and 19 females, with a mean age of 61.5±11.37 years and a mean BMI of 27.72±15.25.The smoking status of the patients was determined as a mean of 42.71±24.54 packet/year. No significant difference was determined between the genders in respect of weight, BMI, FVC%, and FEV1%. The GOLD classification groups were as follows; GOLD A: 22 patients (27.5%), GOLD B: 21 (26.3%), GOLD C: 19 (23.8%), and GOLD D:18 (22.5%). The mild-moderate COPD (GOLD A-B) group included 43 (53.75%) patients and the severe COPD (GOLD C-D) group, 37 (46.25%) patients (Table 1).

Evaluation of body composition on thoracic CT in COPD patients

In the COPD patients, PMA was measured as 40.41±12.51 cm^2, PMI as 14.10±4.18 cm^2/m^2, PMD as 29.52±10.19, SAT area as 42.08±28.89 cm^2, and MAT area as 12.56±7.28 cm^2. (Table 1). A statistically significant difference was determined between the mild-moderate COPD group (GOLD A-B), and the severe COPD group (GOLD C-D) in respect of PMA, PMI and PMD values (p=0.001). A statistically significant difference was determined between the two groups in respect of the SAT and MAT values (p=0.001, p=0.002, respectively). No difference was determined between the groups in respect of cigarette smoking (p=0.265). A statistically significant difference was determined between the two groups in respect of BMI (p=0.01) (Table 2).

Table 1. Baseline characteristics of the patients with COPD

		COPD (n:80)
Sex	**male**	73(91.3%)
	female	7(8.8%)
Age, years		61.05±11.37
Height, cm		1.69±0.07
Weight, kg		79.61±15.25
BMI, kg/m²		27.72±15.25
Smoking history pack/years		42.71±24.54
GOLD stage	**A**	22(27.5%)
	B	21(26.3%)
	C	19(23.8%)
	D	18(22.5%)
FEV1 (% predicted)		67.51±16.51
FEV1/FVC		59.15±10.36
PMA (cm^2)		40.41±12.51
PMI (cm^2/m^2)		14.10±4.18
PMD (HU)		29.52±10.19
SAT (cm^2)		42.08±28.89
MAT (cm^2)		12.56±7.28

PMA: Pectoral muscle area, PMI: Pectoral muscle index, PMD: Pectoral muscle density, SAT: Subcutaneous adipose tissue, MAT Mediastinal adipose tissue, BMI: body mass index

Table 2. Characteristics of the mild-moderate and severe COPD patients

	GOLD A-B (n:43)	GOLD C-D (n:37)	p
PMA (cm^2)	46.72±13.04	33.08±6.52	<0.001
PMI (cm^2/m^2)	15.91±4.22	11.99± 3.01	<0.001
PMD (HU)	36.79±4.62	21.07±8.17	<0.001
SAT (cm^2)	30.37±16.67	55.69±33.95	<0.001
MAT (cm^2)	10.31±5.54	15.17±8.22	0.002
BMI	26.43±4.14	29.23±5.32	0.01
Smoking history pack/years	40.21±18.29	45.62± 24.74	0.265

PMA:Pectoral muscle area, PMI:Pectoral muscle index, PMD: Pectoral muscle density, SAT: Subcutaneous adipose tissue, MAT: Mediastinal adipose tissue, BMI: body mass index

Table 3. ROC analysis of the diagnostic performance of BMI and quantitative body composition parameters according to the ROC analysis for the prediction of the clinical severity of mild-moderate and severe COPD patients according to the GOLD ABCD classification

AUC		Sensitivity (95% CI)	Specificity (95% CI)	Cut-Off
PMA	0.833(0.747-0.918)	67.4	79.4	<38.54
PMI	0.785 (0.685-0.885)	60.5	89.2	<15.06
PMD	0.964 (0.928-1)	93	92	<30.04
SAT	0.755 (0.648-0.862	64.9	79.1	>42.85
MAT	0.677 0.648-0.862)	56.8	76.7	>12.78
BMI	0.658 (0.537-0.780)	59.5	62.1	>29.05

PMA:Pectoral muscle area, PMI:Pectoral muscle index, PMD: Pectoral muscle density, SAT: Subcutaneous adipose tissue, MAT: Mediastinal adipose tissue, BMI: body mass index

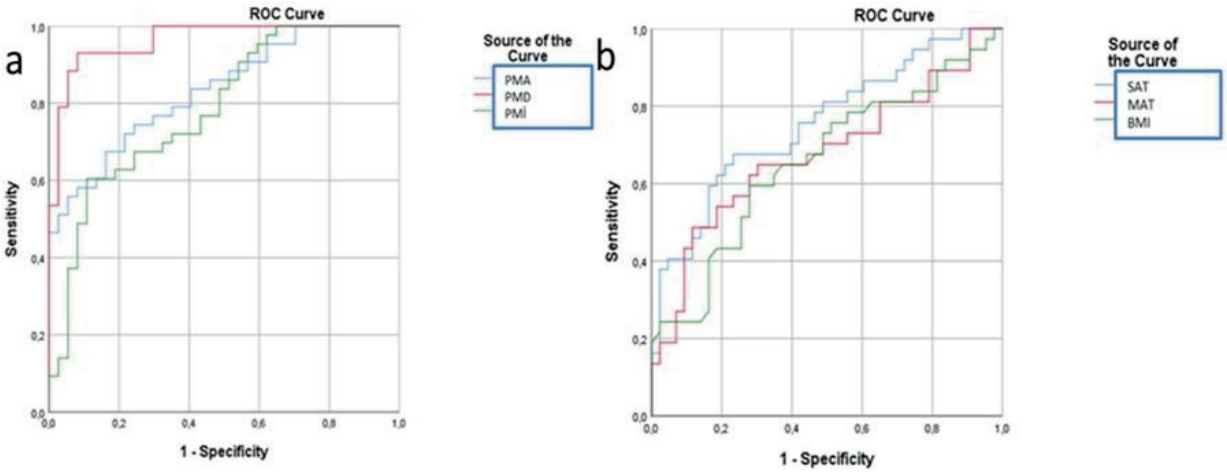

Figure 3. Evaluation of the performance of quantitative body composition values on thoracic CT in the Adifferentiation of mild-moderate (GOLD A-B) and severe (GOLD C-D) COPD.

Evaluation of the performance of the body composition values on thoracic CT according to GOLD ABCD

The best performance in predicting the mild-moderate COPD patients (GOLD A-B) was shown by PMD with a cutoff value of <30.04 (0.964; 95% CI:0.928-1) with a sensitivity of 92% and specificity of 93%, and the lowest performance was shown by PMI with a cutoff value of <15.06 (0.785; 95% CI:0.685-0.885) with 89.2% sensitivity and 60.05% specificity. The best performance in the prediction of severe COPD patients (GOLD C-D) was shown by SAT with a

cutoff value of >42.85 (0.755; 95% CI:0.648-0.862) with 79.1% sensitivity and 64.9% specificity, and the lowest value was BMI with a cutoff value of >29.05 (0.658; 95% CI:0.537-0.780) with 62.1% sensitivity and 59.5% specificity (Table 3, Figure 3).

Discussion

The results of this study demonstrated that body composition measurements on thoracic CT can be used to differentiate mild-moderate and severe disease in COPD patients. A statistically significant difference was determined between mild-moderate and severe COPD patients in respect of the PMA, PMI, SAT, and MAT values measured at the level of the aortic arch ($p<0.05$). The PMD value showed the best performance in the prediction of mild-moderate COPD patients. The well-known simple approach used in this study was the measurement of single cross-sectional areas on thoracic CT scans to evaluate the pectoralis muscle and subcutaneous fat content [8]. Skeletal muscle mass is a lifetime predictor of outcomes related to COPD [5,13]. It has been reported that PMA determined with bio-electric impedance analysis (BIA) in healthy subjects on a single CT image is related to total skeletal muscle mass [14].

Several studies in the literature have examined the relationship between low muscle mass and mortality in different populations with different pulmonary diseases including COPD, cancer, idopathic pulmonary fibrosis and surgical outcomes [15-27]. The majority of measurements derived from CT show a correlation with the severity of the health status. It is important that both qualitative and quantitative skeletal muscle loss is referred to with the term sarcopenia in these studies. However, muscle quality shows information much more relevant to the prediction of patient health and outcomes than the amount of muscle [16-18]. Lipid accumulation in muscles is seen on CT as low muscle density, and fatty accumulation in muscles is known to decrease strength independently of muscle mass [28]. Bak et al. [29] evaluated the effect of PMA and PMD to determine correlations between COPD severity and changes in longitudinal lung function in COPD patients. A relationship was determined between parameters derived from CT and initial pulmonary function and the severity of emphysema ($p<0.05$). In a study by Park et al. [15], CT histogram analysis was used to obtain quantitative measurements from the intercostal muscles and the latissimus dorsi muscle to show fatty infiltration within the muscle. These analyses were correlated with the severity of COPD, and it was determined that intercostal muscle mass decreased and intercostal fatty tissue increased associated with worsening COPD severity. In the same study, intercostal muscle mass adjusted according to BMI was observed to be significantly higher in GOLD A than in GOLD C and D patients, and thus it was reported that intercostal muscle mass could be a marker of COPD severity. A moderate level correlation was also shown in that study between COPD severity and intercostal muscle fat content [15]. McDonald et al. evaluated the relationship between PMA on CT and COPD morbidity. A significant relationship was determined between PMA and parameters related to COPD such as spirometric measurements, shortness of breath, and walking distance [13]. Similarly, in the current study, PMA, PMI, and PMD were determined to be related to COPD severity. When the patients were grouped according to the GOLD classification; PMA, PMI, and PMD were observed to be statistically significantly lower in the severe COPD group (GOLD C-D) than in the mild-moderate COPD group (GOLD A-B) ($p<0.001$). However, as there was no long-term follow up of these patients, the relationship with morbidity and mortality could not be evaluated.

In the study by McDonald et al. [13], PMA was related to the GOLD grade, and there was evidence of a more statistically significant relationship of COPD severity with these measurements than with BMI. In the current study, PMD and PMA showed the best performance in the differentiation of mild-moderate and severe COPD patients. In a study by Furutate et al, the SAT value was reported to be negatively correlated with emphysema progression over a 6-year period ($p<0.01$). In the same study, visceral adipose tissue did not decrease with the severity of emphysema, and showed a positive correlation with the degree of dyspnea [30]. Grace et al. [31] reported that increased subcutaneous thoracic adipose tissue was less related to the progression of emphysema over time in smokers, and increased mediastinal adipose tissue volume was related to a decreased walking distance and increased interleukin-6 (IL-6) levels. In the same study, there was reported to be no significant correlation of IL-6 and C-Reactive Protein (CRP) levels with the longitudinal change in the percentage of pulmonary emphysema or pulmonary function, and walking test. In the current study, the SAT and MAT values were observed to be statistically significantly higher in severe COPD patients than in the mild-moderate group ($p=0.001$, $p=0.002$, respectively). However, biomarkers such as IL-6 and CRP were not evaluated in this study. To be able to evaluate changes occurring in MAT, it can be considered necessary to

evaluate inflammatory changes associated with COPD severity or changes associated with smoking together. Therefore, there is a need for further studies.

There were some limitations to this study, primarily the retrospective design and the low number of patients. A second limitation was the lack of a control group, and the third, comorbidities other than COPD that could affect body composition were not known. In addition, as there was no long-term follow-up, the mortality risk could not be investigated. Finally, in the SAT measurement in female patients, breast fatty tissue in the cross-sectional area could have caused a higher measurement of SAT in some patients.

Conclusion

In conclusion, body composition can be evaluated quantitatively in routine follow-up on thoracic CT in COPD patients without any additional radiation. In addition, the results of this study showed that that the quantitative body composition values measured with thoracic CT can be used in the differentiation of mild-moderate and severe disease in COPD patients. The results also demonstrated that PMD showed the best quantitative body composition performance in the differentiation of mild-moderate and severe COPD patients. Nevertheless, there is a need for further prospective, long-term studies of the use of thoracic CT in the evaluation of body composition.

Funding
The authors declared that this study has no financial support.

Conflict of interest
The authors have no conflicts of interest declared.

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HEALTH SCIENCES QUARTERLY

Volume : 1
Issue : 2
2021

E-ISSN: 2791-6022
https://journals.gen.tr/jsp

Received: 2021-05-12

Accepted: 2021-06-17

REVIEW

Abu Al Qasim Al Zahrawi (Albucasis): The father of modern surgery

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Abstract

Known as the father of surgery, Al-Zahrawi (936-1013AD) made significant contributions to modern medicine and surgery. His greatest contribution to science was his work "Kitab al-Tasrif", which he shared nearly fifty years of experience and medical education by writing and illustrating. In this study, he explained not only surgical interventions, but also the methods and surgical instruments developed by him for the diagnosis, treatment and care services of medicine. In the last chapter of Al-Tasrif consisting of 30 volumes, "On Surgery and Tools", he introduced many surgical instruments such as scalpels, forceps, retractors, curettes, pincers, specula, cauterization, and binding style instruments. This study aims to provide an overview of Al-Zahrawi's life whose contributions to science living in medieval Islamic geography are not limited to modern medicine care services and surgery.

Keywords: *Abu al-Qasim Al-Zahrawi, Albucasis, Kitab al-Tasrif, the father of modern surgery, modern medicine, care services*

Citation: Pekesen M, Ataman AD, Vatanoglu-Lutz E. Abu Al Qasim Al Zahrawi (Albucasis): The father of modern surgery. Health Sci Q. 2021;2:83-86.
https://doi.org/ 10.26900/hsq.1.2.05

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Introduction

Abu al-Qasim Al-Zahrawi, also known in the West as Albucasis, was a great Arab physician and surgeon of the late 10th and early 11th centuries CE. Abu Al Qasim al-Zahrawi (936-1013AD), one of the most important figures in Medieval Islamic Civilization medical history, was born in Al-Andalus, al-Zahra (Medina Azahara). The full name of Al-Zahrawi was Abū al-Qasim Khalaf ibn al-Abbas al-Zahrawi al-Ansari [1,2]. He spent most of his life in Cordoba, Andalusia (Spain) [1]. Al-Zahrawi is referred to as the "father of modern surgery" for his work laying the foundations of modern medicine and his innovative practices in the field of surgery [1,3]. He devoted his whole life to the advancement of medicine and surgery as a whole. It is known that he continued his studies until two years before his death. However in the years following al-Zahrawi's death, little is known about his life, except for his published work, as al-Zahra was destroyed during the Castile-Andalusian conflict. Al-Zahrawi name is first mentioned in the writings of Abu Muhammad bin Hazm (993-1064 AD), who listed the most important physicians of Spain. However, the first detailed biography of al-Zahrawi is al-umaydi's work titled Cezvat al-Muktabis (On the Andalusian Savants) [4].

The medieval period is known as the golden age due to the scientific developments made by Islamic scientists. During this period, important medical advances were made, during which the foundations of modern medical practices were laid [2]. Al-Zahrawi played a vital role in the development of surgical practices and was considered the greatest surgeon of the Islamic golden age [1,5]. Al-Zahrawi, who studied in Cordoba and took lessons from the masters of this science center, has the title of surgeon who is the most known and whose works are known among muslim surgeons [2]. At that time he invented hundreds of instruments, some of which are still used today, and defined surgical practice [1,5,6].

Al-Zahrawi is known as a scientist who really thought well ahead of his time. Known best for his surgical knowledge and expertise, Al-Zahrawi is also known as a contemporary of Andalusian chemists [7]. He has described surgical techniques for a range of procedures covering modern plastic surgery and various subspecialties. Apart from being a physician and surgeon, Al-Zahrawi is known as an exceptional teacher who enthusiastically teaches medical students. He emphasized the value of physician-patient relationships and the importance of providing treatment and care to patients of all social groups [2]. However, Al-Zahrawi's contributions to science were not limited to these. Al-Zahrawi was a great educator and psychiatrist who pioneered the preparation of drugs through sublimation and distillation in pharmacy and pharmacology, and also devoted time to child education and behavior [7]. Al-Zahrawi also served as the court physician to the Umayyad rulers of Andalusia [4].

Al-Zahrawi's contributions to modern medicine and surgical science

Kitab al-Tasrif

The greatest contribution of al-Zahrawi to medical science is undoubtedly his work titled "et-Tasrîf limen Aceze an'd-Taâlîf", which he wrote towards the end of the 10th century and covered the whole of medicine [3]. Consisting of 30 volumes, Kitab al-Tasrif is known as a compilation of nearly fifty years of medical education and experience [2].

This work, which is the first illustrated surgical thesis, played an important role in the development of modern medicine and surgery in both the Islamic world and the West. Tasrif consists of three parts. The first section is based on cauterization recommendations and wound care in stroke (56 episodes), while the second section is divided into open surgical operations, ophthalmology, and oral diseases (97 episodes). The last part consists of various forms of bone fractures, dislocations and gynecology (35 episodes). In addition to all these, pharmacology, cosmetics, midwifery, psychotherapy and medical chemistry subjects were also included in the work [3,4]. It was used as a textbook in many European universities [8]. This work is known as a fundamental source that has been cited for hundreds of years in Islamic geography and Europe [6].

On Surgery and Instruments

In Al-Tasrif's "On Surgery and Instruments" volume 30, he explained the surgical applications and instruments that have not been mentioned in any book before. Surgery and instruments included dentistry, obstetrics and gynecology, head and neck surgeries, ear, nose and throat surgery, general surgery, urology, ophthalmology, dermatological surgeries, and traumatology [1].

Al-Zahrawi in his book revealed the need to redesign the simple and inadequate tools that have been used in operations for more than a thousand years. Al-Zahrawi described more than 200 surgical and

medical instruments, many of which were his own invention, with drawings and detailed descriptions. He explained in detail what materials these tools, should be made of and how these tools should be used. It is known that many of the surgical instruments described in the work are still in use. Among these tools, it is known that there are many tools used for simple or difficult operations such as cauterization tools, scalpels, special pointed scissors, labor tools, kidney stone tools [6]. Some of the tools made by Al-Zahrawi himself included forceps used in childbirth, a scissor-shaped tool to remove the tonsils without suffocating the patient, a special knife to cut the abscess without feeling sick, various hooks and pincers [9]. Today, the "Kocher's method", which is applied to treat a newly discovered dislocated shoulder, and the "Walcher position", which is used to facilitate difficult births, were described in this work at that time [7]. In addition in this study, experimental procedures and cadaver studies on live animals are also mentioned [9].

The final parts of this valuable work, which paved the way for modern medicine and surgery, have been translated into Latin by Gerard of Cremon in the XII. Century. Later, this translation was translated into Greek and Hebrew in the 15th, 16th and 18th centuries, reproduced many times and became widespread [9]. While this work had a significant impact on Italian and French surgeons, it became the surgical book of medical schools in Salerno and Montpellier [10].

Other Pioneering Contributions

Al-Zahrawi has brought new perspectives and solutions to the diagnosis and treatment of the disease not only in the field of surgery but also in anatomy, physiology, neurology, neurosurgery, orthopedics, gynecology, ophthalmology, and general surgery [3].

Al-Zahrawi made contributions to the management of trauma with new methods used to treat trauma patients in cases such as bleeding, airway obstruction, penetrating abdominal and arrow wounds, among his contributions to modern medicine [11].

Al-Zahrawi has also pioneered many diagnoses in the field of neurosurgery and neurology. He is known that he diagnosed and applied surgical treatments for head traumas, skull fractures, hydrocephalus, subdural effusions, spinal injuries and migraine [4]. He described a surgical procedure for ligation of the temporal artery in migraine. His narratives about the anatomy of the brain regarding neurosurgical operations inspired many neuroscientists at that time and later [8].

He cleverly devised methods in colorectal surgery and modeled them in modern surgical procedures [1]. He recommended cauterization for cleft lip treatment in children to close with fibrosis and scarring [2]. He applied cauterization for the ligation of arterial aneurysms. He is known as the first surgeon to use arterial ligation to stop bleeding. He also applied the method of connecting testicular veins to treat varicocele. He performed amputation to treat limb gangrene. He designed an anesthetic sponge for the first time [3]. The use of catgut invented for internal suture in surgical operations is applied in modern surgery. Al-Zahrawi was the first to treat warts with various cannulas. Al-Zahrawi invented forceps in vaginal delivery and for removing a dead fetus [7].

Al-Zahrawi is known to describe many diseases such as hemophilia, ectopic pregnancy and gynecomastia and focus on their treatments [2,7]. Al-Zahrawi proved that a cut in her throat can heal by treating a slave girl who cut her own throat in a suicide attempt, and gained the experience that a laryngotomy is not dangerous [4]. It is also known that he performed tracheostomy and lithotomy at that time [5].

He treated the hemorrhoids with non-invasive methods. He identified chronic constipation as the cause of the fissure, and suggested flushing the fissure with warm water and applying topical ointment to speed healing. Identified risk factors for hernia and prescribed fast-acting laxatives [1].

It is known that Al-Zahrawi treats inguinal hernia surgically but cares about postoperative care against the side effects of the surgical procedure [12]. He achieved success by identifying neurological symptoms of leprosy [11].

Conclusion

Al-Zahrawi contributed greatly to the advancement of Western European surgery, modern medicine and thus care services. Al-Zahrawi has brought new perspectives and solutions to the diagnosis and treatment of the disease not only in the field of surgery but also in neurology, orthopedics, gynecology, ophthalmology, neurosurgery, and general surgery. In addition, al-Zahrawi stands out with his educator identity outside of medicine. Apart from being a good scholar and psychiatrist, he worked in agriculture, pharmacology, chemistry and cosmetics. Al-Zahrawi is known as the father of modern surgery and the head of all surgeons. Although the term Father of Surgery is attributed to a few people, Al-Zahrawi was a surgeon who deserved this title.

He invented many instruments that were not previously known in Europe, such as surgical applications and double-ended hooks, forceps, catgut, which are still used in modern surgery [4]. Al-Zahrawi's greatest contribution to science was his work called "et-Tasrîf limen Aceze an'd-Taalif". In this book of Al-Zahrawi, he introduced more than 200 cutting and piercing surgical instruments such as scalpel, retractor, rake, pincer, specula, which he described visually. These instruments also included a class surgical instrument for cauterization and binding style.

The experience, teachings and principles of Al-Zahrawi, a pioneer in modern medicine and plastic surgery, continue to inspire the diagnosis and treatment of medicine today.

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HEALTH SCIENCES QUARTERLY

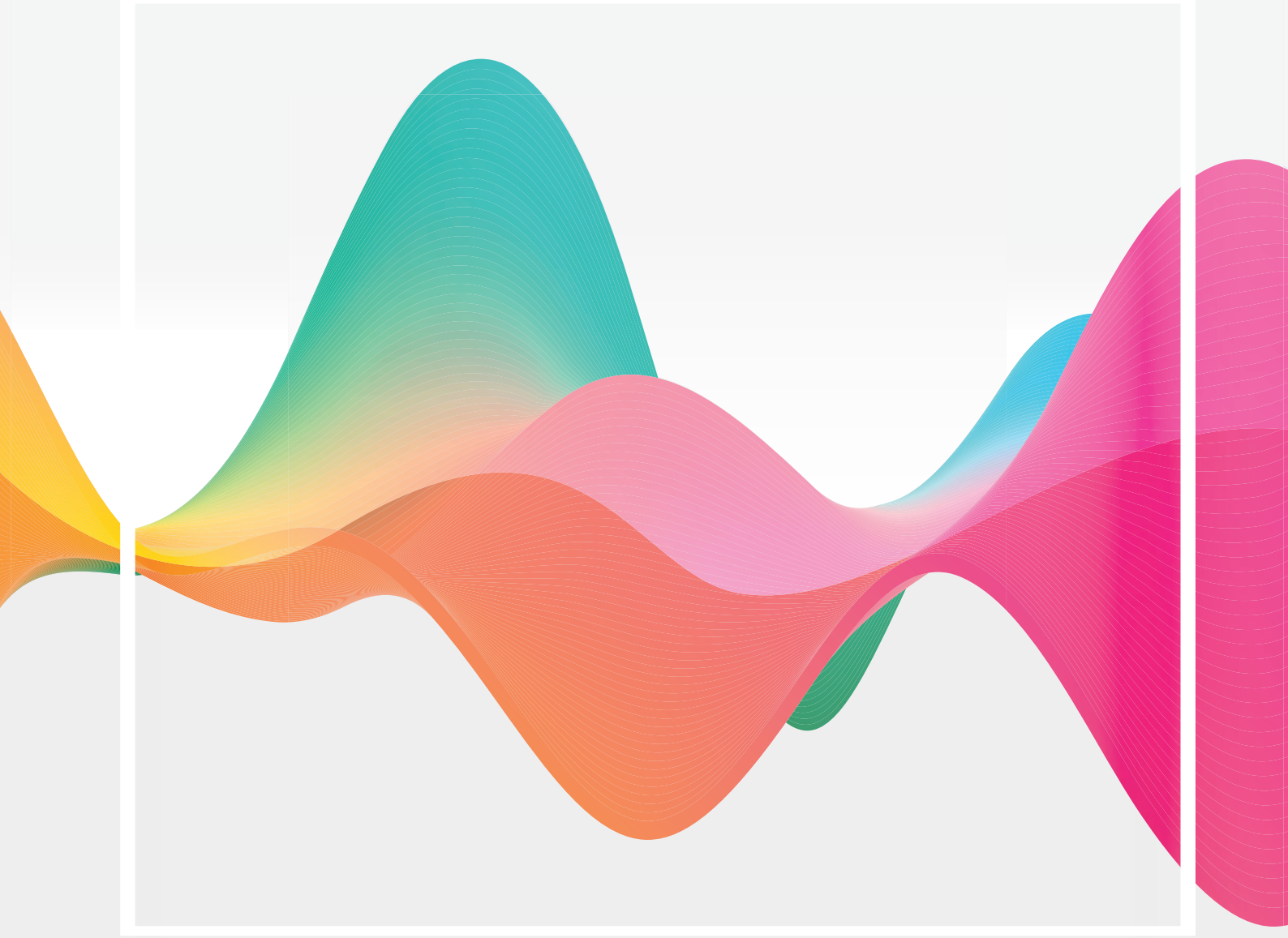
E-ISSN: 2791-6022

DOI: 10.26900/hsq

Volume 1

Issue: 2

2021



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