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Articles

Prejudice, Stigma and the Refusal to Offer Health Services of an Obese Pregnant Woman – An Ethical Viewpoint

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Abstract

Obesity in pregnancy is a medical condition that has short- and long-term negative consequences for the mother as well as for the child. Therefore, it is a necessity that these women are informed and educated about their condition as well as should be actively encouraged to reduce weight. Because of the negative social stereotype that follows obese persons, they face daily prejudice and stigma in their work, everyday life, and when receiving health services. This paper aimed to present a case, the refusal of the obstetricians to perform a cesarean section on an obese pregnant woman. The refusal was based on the fear of complications during or after the operative intervention, and subsequent consequences that they may imply. Refusing to treat this patient, regardless of the high risk of complications, was unjustified, unfair, and ethically unacceptable. There are no circumstances where the individual status of the patient should be a reason not to offer them the medical services that they need. The medical staff in these cases should have in mind any special medical precautions needed and apply their knowledge aiming an adequate and accurate medical service for every patient. Therefore human values are essential to good medical practice. Health personnel should not claim special moral status that would allow them to deny the patient's right to medical treatment and always show respect for patient autonomy.

Keywords: pregnancy, obesity, stigma, prejudice, discrimination, medical ethics.

1. Introduction

From the start of the 20th century, the surveillance and management of pregnancy and labor are constantly evolving thanks to the advances in technology and modern medical practices. It is known by every obstetrician that timely operative intervention can make the difference between life and death for the baby as well as for the mother. This paper aims to present a case of prejudice, stigma, and discrimination towards a pregnant woman in our Clinic. The stem of bioethics consists of 4 main principles: the autonomy of the patient, acting on the interests of the patient, making sure to do no harm, medical services without bias, or other injustices. We use these four principles in our everyday clinical work when we are faced with a potential ethical question that needs resolving (Beauchamp, Childress, 2001). At the professional level, it is unfair and unethical to

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refuse medical services to an obese person. It is well known that obesity can be accompanied by stigma, prejudice, and discrimination in society, as well as from medical staff, and these can lead to subpar and inadequate medical treatment. Regardless of the weight of the patients, it is the doctors' duty to apply his/her knowledge and best clinical practices while offering medical services to any of their patients, including an obese one. Obesity in itself requires a multidisciplinary approach for its treatment, and an obese pregnant woman can be challenging for the obstetrician. He/she should be familiar with obesity complications during pregnancy, offer a safe treatment while avoiding name-calling (e.g. the fat one, the obese, etc.). Obesity is defined as a condition of being fat with a BMI of over 30 (Shields et al., 2011) and it is classified into 3 classes (Flegal et al., 2013). Over the past decade the number of obese people has dramatically increased throughout the whole globe. The latest studies show that two in five women in the USA are considered overweight (Hales et al., 2017), while 22 % of pregnant women in the UK are obese, 28 % overweight, and 47 % are considered in the normal range of BMI. Discrimination and stigma of a person with obesity in health institutions can have a negative effect while offering medical services, especially in obstetrics and gynecology, because of the nature of gynecological examination (Aldrich, Hackley, 2010). Obesity significantly increases the risk of complications, this includes but not limited to arterial hypertension, hypercholesterolemia, diabetes mellitus, cardiovascular problems, stroke, surgical site infection, etc. (Kundu et al., 2018). During pregnancy, obese women are at an increased risk for recurrent abortions, pregnancy-induced hypertension, pre-eclampsia and eclampsia, gestational diabetes, preterm labor, intrauterine demise, fetal anomalies, fetal macrosomia, difficult labor (shoulder dystocia, technical difficulties while performing operative labor), as well as increased risk of complicates after labor (wound infections, vein thrombosis etc.)(Dudenhausen et al., 2015). Having all this in their minds, it can sometimes happen; not wanting to deal with postoperative complications as well as possible legal implications, obstetricians might not always make the right decision for their obese patient, raising here ethical issues. A similar case we had at our clinic, where some doctors refused to perform Cesarean section in an obese patient, mainly trying to avoid possible legal consequences afterward.

2. Methodology

The case study is a method of empirical inquiry appropriate to the description of phenomena and contributes to understanding phenomena in a holistic and real-life context. This case study is a description of a specific case, where the patient is prejudiced, stigmatized to the point of refusal to be treated by doctors, due to her obese condition. The patient was a pregnant woman and was admitted to our clinic for delivery. Interviews were used as a tool for data collection. The patient is informed in advance about the purpose of the interview and approval was obtained for the publication of data.

Case Presentation

A 37-year-old woman presents to our clinic at 39 + 5 weeks of pregnancy (according to the first day of the last menstrual period). There was no associated pain. During the pelvic exam, she had no extra-uterine bleeding or amniotic fluid leaking. Medical history shows that the patient had no prior births, but she had two spontaneous abortions, which occurred during the first trimester. The patient was treated for infertility for five years. Social history shows that the patient had finished primary education but was unemployed, with a low economic income and no health insurance. She was obese, without physical activity and a heavy smoker (20 pack-years). About the 23rd week of pregnancy, she started treatment with methyldopa for pregnancy-induced hypertension (PIH). The patient states that she has been tested for diabetes in the 26th week of pregnancy, and it resulted negative. The blood pressure was 150/95 mmHg while the heart rate was 91/min. The respiratory rate was 18 breaths per minute, and the body temperature is 37.2 C (99F). On physical examination, her body mass index (BMI) was 39.7 kg/m2, with bodyweight; 108 kg and length; 165cm. She had slight acne on her face and chest. Asked about her body weight, she stated that she gained thirty kilograms (bodyweight) during pregnancy, but even before pregnancy she was overweight. She had tried to lose weight several times but with no success, was demotivated and unwilling to try again. She believes her obesity has its connectivity with her family history, although there was no documentation of any confirmed pathology. During vaginal examination; was found normal uterine activity, the cervix anterior presentation, strong and

completely closed, fetal heartbeat evident and regular. Ultrasonographic examination of the fetal biometry showing an intrauterine growth restriction (asymmetric IUGR) and Doppler velocimetry of umbilical and middle cerebral artery had pathological values. Laboratory analysis: hemogram at the limits of reference values. Urine: no proteinuria. Biochemistry analysis: double transaminases (ALT: 71 U/L, AST: 64 U/L, LDH: 847 U/L), Creatinine: 103 µmol/L, other biochemical analyses at the limits of reference values. Cardiotocography: with decreased variability and no acceleration. Based on the Doppler velocimetry fetal umbilical and middle cerebral artery which was pathological, (asymmetric IUGR), history of infertility and recurrent abortions, as well as other risk factors such as smoking, obesity, pregnancy-induced hypertension, after adequate information on the advantages, disadvantages and possible complications during and after surgery. Cesarean delivery was proposed and consent was given. The operative team is sent for surgery, but after seeing the degree of obesity of the patient, they refuse to give birth to the woman with the Cesarean section, due to fear of the law if any serious complication occurs. The baby was born via Caesarean section two hours later by another operative team: a female infant; bodyweight 2350 grams, 46 cm; Apgar score: 7/8. Five days after the birth by cesarean section, she and her baby were released home in good health with advice and therapy. This refusal to treat a pregnant woman due to obesity is not justified, it was considered unfair and ethically unacceptable.

3. Discussion

In a meta-analysis of papers, Puhl and Brownell concluded that in general all medical staff, including students, has a negative perception for the obese patient (Puhl, Brownell, 2001). In the USA 66 % of obese persons are discriminated against (Andreyeva et al., 2008). This discrimination comes in many forms, not only while receiving health services but also in other settings, like work where they are considered lazy, lacking motivation for work, and less competent (Roehling, 1999). It is thought that this attitude of medical staff comes from the fact that obesity is considered in its core a lack of self-control (over-eating, no or little physical activity etc.) and persons' lack of willingness to do something about it, to work towards weight loss. Regardless of the personal responsibility, many studies show that treatment of obese persons is a multi-factorial process and it should account for noncompliance of the patient, lack of motivation and discipline (Thuan, Avignon, 2005). This mixture of obstacles in treating obesity often translates to a negative perception from medical staff, where they see it as a waste of their time, without an acceptable result. In a study that included 600 medical doctors in France, it was shown that 57 % of them consider their work non-effective on treating patients with obesity (Bocquier et al., 2005). We presented a case where a pregnant woman was avoided by the obstetricians to perform C-Section, due to her obesity. Stigma on treating obese women seems to be a global issue. In their study, Puht and Brownell presented that in 69 % of obese women felt stigmatized at least once during their medical examination, and 52 % have had this happen more than once. Overall, medical services ranked second on the list of 20 places where these patients felt most stigmatized. This attitude of medical workers towards obese women can have a secondary effect, on these women avoiding regular visits (Breast and/or Cervical cancer screening etc.). Therefore, we consider it essential for our medical co-workers and staff to make sure they are offering these patients the necessary and best services possible and to make sure there is no prejudice or discrimination in any form or usage of name shaming, as we should not for any patient. Furthermore, we have to help educate society that health care is a fundamental human right, and as such should be offered without exceptions.

4. Conclusion

It is confirmed that obesity is a medical condition that has a direct negative effect on the health of pregnant women, the fetus, and the social impact. In clinical practice, obese patients often have to deal with stigma, prejudice, and discrimination that can go as far as a refusal to receive medical treatment. We consider it inhumane, in any circumstance, to refuse medical treatment to any person in need. The medical caregivers should have individual principles and make sure to honor their oath for their duty to every person to the best of their knowledge; furthermore, they should refrain from taking a higher moral stance. The treatment of any obese patient, including pregnant women, requires patient and careful treatment. Our refusal to treat them is against our call and unethical. It is necessary to inform obese pregnant women about their condition and what it means for the pregnancy and the baby. Careful explanations of the mode of birth also help

prepare her for possible in-labor and/or post-partum complications. All of this should be done while encouraging and helping lose weight. Good communication between patients and their caregivers should be supported by good and proven medical practices. The situation, as in our case, should not happen and should not be allowed to repeat itself. This sort of refusal is unjustified and ethically unacceptable. Society should embrace the notion of health as an inalienable fundamental human right and as such it should be our (medical staff) duty and privilege to make sure this right is respected.

5. Author's contributions

Astrit M. Gashi; analyzes the case, reviews the literature, and compiles the manuscript. All authors have read and approved the final version of the manuscript.

6. Conflict of interest

The authors report no conflict of interest in this case presentation.

Additional information

Informed consent

Informed written consent is provided by the patient to publish the case details. No institutional approval is required to publish this case.

References

Aldrich, Hackley, 2010 – Aldrich, T., Hackley, B. (2010). The impact of obesity on gynecologic cancer screening: an integrative literature review. Journal of midwifery & women's health. 55(4): 344-356.

Andreyeva et al., 2008 – Andreyeva, T., Puhl, R.M., Brownell, K.D. (2008). Changes in perceived weight discrimination among Americans, 1995–1996 through 2004–2006. *Obesity*. 16(5): 1129-1134.

Beauchamp, Childress, 2001 – Beauchamp, T.L., Childress, J.F. (2001). Principles of biomedical ethics. Oxford University Press, USA.

Bocquier et al., 2005 – Bocquier, A., Verger, P., Basdevant, A., Andreotti, G., Baretge, J., Villani, P., Paraponaris, A. (2005). Overweight and obesity: knowledge, attitudes, and practices of general practitioners in France. Obesity Research. 13(4): 787-795.

Dudenhausen et al., 2015 – Dudenhausen, J.W., Grünebaum, A., Kirschner, W. (2015). Prepregnancy body weight and gestational weight gain—recommendations and reality in the USA and in Germany. *American Journal of Obstetrics & Gynecology*. 213(4): 591-592.

Flegal et al., 2013 – *Flegal, K.M., Kit, B.K., Orpana, H., Graubard, B.I.* (2013). Association of all-cause mortality with overweight and obesity using standard body mass index categories: a systematic review and meta-analysis. *Jama*. 309(1): 71-82.

Hales et al., 2017 – *Hales, C.M., Carroll, M.D., Fryar, C.D., Ogden, C.L.* (2017). Prevalence of obesity among adults and youth: United States, 2015–2016.

Kundu et al., 2018 – Kundu, S., Karakas, H., Hertel, H., Hillemanns, P., Staboulidou, I., Schippert, C., Soergel, P. (2018). Peri-and postoperative management and outcomes of morbidly obese patients (BMI> 40 kg/m 2) with gynaecological disease. Archives of gynecology and obstetrics. 297(5): 1221-1233.

Puhl, Brownell, 2001 – Puhl, R., Brownell, K.D. (2001). Bias, discrimination, and obesity. *Obesity research*. 9(12): 788-805.

Roehling, 1999 – *Roehling, M.V.* (1999). Weight-based discrimination in employment: Psychological and legal aspects. *Personnel Psychology*. 52(4): 969-1016.

Shields et al., 2011 – *Shields, M., Carroll, M.D., Ogden, C.L.* (2011). Adult obesity prevalence in Canada and the United States. US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics.

Thuan, Avignon, 2005 – *Thuan, J.F., Avignon, A.* (2005). Obesity management: attitudes and practices of French general practitioners in a region of France. *International journal of obesity*. 29(9): 1100-1106.

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Assessment of Left Ventricular Systolic Function after Acute Myocardial Infarction by Tissue Doppler Imaging

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Abstract

The coronary artery disease is the leading cause of mortality and morbidity globally and acute myocardial infarction is the commonest mode of presentation. The tissue Doppler imaging shows myocardial motion (measured as tissue velocity) at specific locations in the heart.

Tissue velocity indicates the rate at which a particular point in the myocardium moves toward or away from the transducer. Integration of velocity over time yields displacement or the absolute distance moved by that point. The most common method for determining ventricular volumes is the Simpson rule, or the "rule of disks." This technique requires recording an apical, four- and/or two-chamber view from which the endocardial border is outlined in end-diastole and end-systole. A cross-sectional study carried out in The AL-Kindey Teaching Hospital (November 2017 – July 2018), 60 patients, 39 (65 %) males and 21(35 %) females with acute myocardial infarction of first time admitted to CCU. All patient were admitted to Coronary Care Unit and Left Ventricular systolic function had been evaluated by measuring Systolic myocardial velocity (sm) by Pulse Wave tissue Doppler imaging and Ejection Fraction by Simpson's method.

Results revealed that 25 patients (41.7 %) of them presented with anterior Myocardial infarction, inferior Myocardial infarction in 17 patients (28.3 %), lateral Myocardial infarction in 11 patients (18.3 %), and septal Myocardial infarction in 7 patients (11.7 %). (60.6 %) of anterior Myocardial infarction, (24.2 %) of inferior Myocardial infarction, (9.1 %) of lateral Myocardial infarction, and (6.1) of septal Myocardial infarction were associated with Ejection Fraction <55.

There were significant differences between means of 4 mitral annular sites Sm by ejection fraction for patients with anterior, lateral Myocardial infarction, and septal Myocardial infarction.

Keywords: myocardial infarction, tissue doppler imaging, left ventricular ejection fraction.

1. Introduction

Coronary artery disease is the leading cause of mortality and morbidity globally and acute myocardial infarction is the commonest mode of presentation. In patients with acute myocardial infarction heart failure is characterized either by systolic dysfunction alone or by both systolic and diastolic dysfunction (Goldberg et al., 2006).

Myocardial infarction (MI) can be recognized by clinical features, including electrocardiographic (ECG) findings, elevated values of biochemical markers (biomarkers) of myocardial necrosis, and by imaging, or may be defined by pathology. It is a major cause of death

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and disability worldwide. MI may be the first manifestation of coronary artery disease (CAD) or it may occur, repeatedly, in patients with established disease (Thygesen et al., 2012).

The tissue Doppler imaging shows myocardial motion (measured as tissue velocity) at specific locations in the heart. Tissue velocity indicates the rate at which a particular point in the myocardium moves toward or away from the transducer. Integration of velocity over time yields displacement or the absolute distance moved by that point (Zaca et al., 2010).

2. Materials and methods

Tissue Doppler Imaging

Tissue Doppler imaging (TDI) is a novel use of ultrasound to image the motion of tissue with Doppler echocardiography. Doppler echocardiography records and displays the velocities of the moving targets. The Principles of TDI; Doppler echocardiography relies on detection of the shift in frequency of ultrasound signals reflected from moving objects. With this principle, conventional Doppler techniques assess the velocity of blood flow by measuring high-frequency, low-amplitude signals from small, fast-moving blood cells. In TDI, the same Doppler principles are used to quantify the higher amplitude, lower-velocity signals of myocardial tissue motion. There are important limitations to TD interrogation. TDI can be performed in pulsed wave and color modes. Pulsed-wave TDI is used to measure peak myocardial velocities and is particularly well suited to the measurement of long-axis ventricular motion because the longitudinally oriented endocardial fibers are most parallel to the ultrasound beam in the apical views. Because the apex remains relatively stationary throughout the cardiac cycle, mitral annular motion is a good surrogate measure of overall longitudinal LV contraction and relaxation (Galiuto et al., 2002).

To measure longitudinal myocardial velocities, the sample volume is placed in the ventricular myocardium immediately adjacent to the mitral annulus. The cardiac cycle is represented by 3 wave forms:

(1) Sm, systolic myocardial velocity above the base- line as the annulus descends toward the apex.

(2) Ea, early diastolic myocardial relaxation velocity below the baseline as the annulus ascends away from the apex.

(3) Aa, myocardial contraction velocity associated with atrial. The lower-case "a" for annulus or "m" for myocardial (Ea or Em) and the superscripted prime symbol (E') are used to differentiate tissue Doppler velocities from conventional mitral inflow. Pulsed-wave TDI has high temporal resolution but does not permit Simultaneous analysis of multiple myocardial segments. With color TDI, a color-coded representation of myocardial velocities is superimposed on gray-scale 2-dimensional or M-mode images to indicate the direction and velocity of myocardial motion. Color TDI mode has the advantage of increased spatial resolution and the ability to evaluate multiple structures and segments in a single view (Edvardsen et al., 2001). From TDI uses are:

Assessment of Myocardial Relaxation:-

Early diastolic velocity (Em and Am) of the mitral annulus measured with TDI is a good indicator of LV myocardial relaxation. This is one of the most important components of myocardial diastolic function the mitral annulus can be appreciated visually from the parasternal long-axis and apical four-chamber views, but TDI records and demonstrates the velocity of the longitudinal motion in numerical value (Otto et al., 2013).

Estimation of Left Ventricular Filling Pressure:

LV diastolic filling pressures can be estimated reliably with 2D and Doppler echocardiography. The deceleration time (DT) of mitral inflow early diastolic velocity (Em) has a good inverse correlation with the pulmonary capillary wedge pressure (PCWP) of less than 130 milliseconds usually indicate a PCWP greater than 20 mm Hg. However, mitral inflow DT alone is not highly accurate in patients who have a relatively normal LVEF or atrial fibrillation. Because Em is reduced in patients with impaired relaxation and is affected less by preload than mitral inflow E, the ratio (E/Em) between mitral inflow early diastolic velocity and mitral annulus early diastolic velocity increases as PCWP increases (Takashioki, 2003).

Evaluation of Regional and Global Systolic Function:

Assessment of LV Systolic Function: Systolic myocardial velocity (Sm) at the lateral mitral annulus is a measure of longitudinal systolic function and is correlated with measurements of LV ejection fraction and peak dP/dt. A reduction in Sm velocity can be detected within 15 seconds of

the onset of ischemia and regional reductions in Sm are correlated with regional wall motion abnormalities (Alam et al., 2007). Incorporation of TDI measures of systolic function in exercise testing to assess for ischemia, viability, and contractile reserve has been suggested because peak Sm velocity normally increases with dobutamine infusion and exercise and decreases with ischemia (Marwick et al., 2004). The present study aimed to evaluate the Systolic myocardial velocity (Sm) and its relation to ejection fraction (EF) by Simpson's method in first acute myocardial infarction.

Patients and Method

A cross-sectional study carried out in The AL-Kindy Teaching Hospital (November 2017 - July 2018). The study duration was 8 months and was approved by hospital ethical committee, Number of people were included 60 patients, 39 (65 %) males and 21(35 %) females, aged from 45 to 60 years with acute myocardial infarction of first time admitted to CCU. All patient were admitted to CCU and LV systolic function had been evaluated by measuring Sm by PW tissue Doppler imaging and EF by Simpson's method. All patients were in sinus rhythm.

The diagnosis of MI was based on the following criteria:

Characteristic chest pain, ECG changes and positive test (Galiuto et al., 2002).

Evaluation of LV EF <55 % suggested LV systolic dysfunction ^[10,11]. Then pulsed wave TDI was performed on four different sites on the mitral annulus i.e. lateral, septal, anterior and inferior. For lateral and septal sites apical 4-chamber view and for anterior and inferior sites apical 2-chamber view was used.

3. Results

Sixty patients with acute first myocardial infarction were included. The mean age was (53.03 ± 4.64) years as shown in Table 1, there were 39 males (65 %) and 21 females (35 %) as shown in Figure 1.

Note: A p-value of \leq 0.05 was considered as significant.

Table 1. Mean ± SD of age of all study patients



Fig. 1. Distribution of patients according to gender

Figure 2 shows the distribution of patients according to type of myocardial infarction. Majority 25 patients (41.7 %) of them presented with anterior MI, inferior MI in 17 patients (28.3 %), lateral MI in 11 patients (18.3 %), and septal MI in 7 patients (11.7 %).



Fig. 2. Distribution of patients according to type of MI

Table 2 shows the association between type of myocardial infarction and ejection fraction [<55 % (impaired LV systolic function) or \geq 55 % (normal LV systolic function)], (60.6 %) of anterior MI, (24.2 %) of inferior MI, (9.1 %) of lateral MI, and (6.1) of septal MI were associated with EF <55 and there was a significant association between type of MI and EF, p = 0.006.

	Ejection		
Variable	LV dysfunction (<55 %)	Normal function (≥55 %)	P-value
			Type of MI
Anterior	20 (60.6 %)	5 (18.5 %)	
Inferior	8 (24.2 %)	9 (33.3 %)	
Lateral	3 (9.1 %)	8 (29.6 %)	0.006
Septal	2 (6.1 %)	5 (18.5 %)	
Total	33 (100 %)	27 (100 %)	

Table 2. The association between type of MI and ejection fraction

Figure 3 shows the correlation between mean Sm velocity and ejection fraction among patients with MI. There was a significant positive linear correlation between these two variables (r = 0.787, P-value = <0.001).



Fig. 3. The correlation between mean systolic mitral annular velocity and ejection fraction

Figure 4 illustrated the differences of the mean mitral Sm velocity assessed by Doppler tissue imaging at different sites of the mitral annular among patients with anterior MI. There was difference between means of Sm at 4 mitral annular sites with significant reduction in ant and septal mitral annular Sm (6.136, 6.86 respectively) than other mitral annular sites [inferior and lateral (8.172, 7.524 respectively)] among patients with anterior MI (Friedman test P-value < 0.001).



Fig. 4. The means of the Sm at 4 mitral annular sites among patients with anterior MI

Figure 5 shows the differences of Mean mitral Sm velocity assessed by Doppler tissue imaging at different sites of the mitral annular among patients with inferior MI. There was significant reduction of mean Sm of inferior and septal mitral annular sites (6.041, 8.429 respectively) than other [lat and ant mitral annular sites (9.429, 9.211 respectively)] among patients with inferior MI (P-value < 0.001).



Fig. 5. The means of the Sm at 4 mitral annular sites among patients with inferior MI

Figure 6 shows the differences of Mean mitral Sm velocity assessed by Doppler tissue imaging at different sites of the mitral annular among patients with lateral MI. There was significant reduction of mean Sm of lateral mitral annular site (5.845) than other mitral annular sites among patients with lateral MI (P-value < 0.001).



Fig. 6. The means of the Sm at 4 mitral annular sites among patients with lateral MI

Figure 7 shows the differences of Mean mitral Sm velocity assessed by Doppler tissue imaging at different sites of the mitral annular among patients with septal MI. There was a significant reduction of mean Sm of septal mitral annular site (5.257) than other mitral annular sites among patients with septal MI (P-value < 0.001).

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Fig. 7. The means of the Sm at 4 mitral annular sites among patients with septal M

Table 3 shows the mean differences of mean mitral annular peak systolic velocities (Sm) of all 4 mitral annular sites by ejection fraction among patients with MI. There were significant differences between means of 4 mitral annular sites Sm by ejection fraction for patients with anterior, lateral MI, and septal MI (p value < 0.001, 0.006, 0.016 respectively).

Table 3. The means of the mitral annular peak systolic velocities (Sm) of all 4 mitral annular sites by ejection fraction among patients with anterior, lateral and septal MI

Type of MI	Categories %	Ν	Mean \pm S.D	t-test	P value
Antonion MI	LV dysfunction (<55)	20	6.93 ± 0.68	- 5 0 0 0	<0.001
AIITCHOI MI	Normal function (≥ 55)	$n (\ge 55) 5 8.10 \pm 0.36$	8.10 ± 0.36	-5.233	<0.001
	LV dysfunction (<55)	3	8.05 ± 0.27		
Lateral MI	Normal function (≥ 55)	8	8.92 ± 0.38	-3.57	0.006
Septal MI	LV dysfunction (<55)	2	7.51 ± 0.08		
	Normal function (≥ 55)	5	8.69 ± 0.44	-3.569	0.016

Table 4 shows the mean differences of mean mitral annular peak systolic velocities (Sm) of all 4 mitral annular sites by ejection fraction among patients with inferior MI, and there was significant association between mean Sm and EF (p value 0.001).

Table 4. The means of mitral annular peak systolic velocities (Sm) of all4 mitral annular sites by ejection fraction among patients with inferior MI

Type of MI	Categories	Ν	Mean Rank	Z	P value
	LV dysfunction (< 55 %)	8	4.75		
Inferior MI				-3.274	0.001
	Normal function(≥ 55 %)	9	12.78		

Mann-Whitney test

4. Discussion

In the present study, acute first myocardial infarction was shown to occur 1.6 time more in male in comparison with female but it was statistically insignificant (P-value 0.285).

When we divided the MI patients into those with anterior or inferior, lateral and septal MIs, we found lower mitral annular velocity at sites of infarction (P-value < 0.001).

There was significant association between type of MI and EF, p value 0.006.

A significant regional difference was found in the peak systolic velocity at the mitral annulus related to the infarction site (P-value < 0.001). The similar pattern has been reported by Salehi et al. (2010).

In current study, the acute anterior MI was the more frequent among MI cases, accounted (41.7%) of all patients. The patients with acute anterior MI had Sm reduction of all four mitral annular sites with significant reduction in anterior and septal mitral annular Sm than other mitral annular sites (inferior and lateral) (P-value < 0.001). These findings agreed that of previous study done by Rahman et al. (2011) who showed significant reduction in anterior and septal mitral annular Sm than other mitral annular Sm than other mitral annular Sm than other mitral annular sites (inferior and lateral) in patients with acute anterior MI.

In our study, patients with acute anterior MI were divided into two groups according to an ejection fraction, those with EF (<55 %) and (≥55) as LV systolic dysfunction and normal LV systolic function respectively (Ommen et al., 2000; Otto et al., 2013a) and it was seen that majority (80 %) of anterior MI patients, which constituted (60.6 %) of all patients had LV systolic dysfunction, Although the myocardial velocity and ejection fraction are two different measurements, there was significant correlation between mean Sm reduction of all four mitral annular sites and EF (p value < 0.001), These findings agreed that reported by Rahman et al., (2011) who reported LV systolic dysfunction in 82 % of ant MI patients and 79 % among all patients with LV systolic dysfunction. This correlation between the mean mitral annular systolic velocity and LV ejection fraction indicates that systolic velocity plays an important role in the pumping function of the left ventricle.

In the present study, the patients with acute inferior MI represented 28.3 % of all patients. The patients with inferior MI had lower Sm of all four mitral annular sites with significant reduction in inferior mitral Sm and septal mitral Sm (P < 0.001), and this reduction of septal Sm may be due to partial damage to the septum in inferior MIs, as the posterior part of the septum is usually supplied by the right coronary artery (Salehi et al., 2010).

When the inferior MI patients were divided in to those with EF (≥ 0.55) and those with EF (<55 %), we found 47 % among patients with inferior MI which constituted 24.2 % of all patients had been impaired LV systolic function and there was significant correlation between mean Sm and EF (p value = 0.001), this has been reported by Rahman et al. (2011) but with LV systolic dysfunction was found in 22 % of patients with acute inferior MI and 20 % of all MI patients with LV systolic dysfunction, and the cause of this variation was thought to be due to higher no. of patients in study(200 patients).

In current study, patients with lateral MI represented 18.3 % of all patients. Those had Sm reduction at the non-infarction sites, in addition to Sm reduction at the infarction sites, and there was significant reduction of peak lateral mitral annular Sm velocity (p value < 0.001). The similar pattern has been reported by Alam et al. (2000).

From other point of view, the mean Sm of all mitral annular sites patients with lateral MI was significantly low (p value < 0.001). Similar observation had reported by Alam et al. (2000).

In our study 9.1% of patients with lat. MI had LV systolic dysfunction, and there was significant correlation between mean Sm and EF in patients with lat. MI (p value = 0.006). These findings agreed that of study done by Esmailzadeh et al. (2009) (p value < 0.001).

While patients with septal MI represented 11.7 % of all patients in the study. In addition to the Sm reduction at the infarction sites, Sm at the non-infarction sites was also reduced as compared with healthy subjects, and there was significant lower peak septal Sm velocity (p value < 0.001). This finding was similarly reported by Alam et al. (2000).

From other point of view, the mean Sm of all mitral annular sites was significantly reduced in septal MI (p value < 0.001). Similar observation has been reported by Alam et al. (2000).

LV systolic dysfunction was found in 28 % of patients with septal MI which constituted 6.1 % of all MI patients with impaired LV systolic function, and there was significant correlation between mean Sm and EF in patients with septal MI (p value = 0.03). This finding was similarly reported by Esmailzadeh et al. (2009).

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In current study, 55 % of all patients had been found with LV systolic impairment and associated with a significant reduction of mean Sm of four mitral annular sites (p value < 0.001). These findings agreed that of previous study done by Zaca et al. (2010).

In the present study, there has been relatively significant positive linear correlation between mean Sm and EF (r = 0.787, P < 0.001), as in Figure 6, this is similarly reported by Rahman et al., (2011) with (r = 0.74, P < 0.001).

References

Alam et al., 2007 – *Alam, M. et al.* (2007). Detection of abnormal left ventricular function by Doppler tissue imaging in patients with a first myocardial infarction and showing normal function assessed by conventional echocardiography. *Eur J Echocardiography.* 8: 37-41.

Alam, 2000 – *Alam, M.* (2000). The effect of a first myocardial infarction on the systolic and diastolic velocity profiles of the mitral annulus determined by pulsed wave Doppler tissue imaging. *Journal of the American Society of Echocardiography.* 346-347.

Edvardsen et al., 2001 – *Edvardsen, T. et al.* (2001). Regional myocardial systolic function during acute myocardial ischemia assessed by tissue Doppler echocardiography. *J Am CollCardiol.* 37: 726-730.

Esmailzadeh, 2009 – Esmailzadeh, M. (2009). Evaluation of regional systolic myocardial function in the early stage of acute myocardial infarction by strain rate imaging. Iranian Cardiovascular Research Journal. 3(4): 181-90.

Galiuto et al., 2002 – *Galiuto et al.* (2002). Contraction and relaxation velocities of the normal left ventricle using pulsed-wave tissue Doppler echocardiography. *Am J Cardiol.* 81: 609-614.

Goldberg et al., 2006 – *Goldberg, J.R. et al.* (2006). Trends in community mortality due to coronary heart disease. *Am Heart J.* 151(2): 501-7.

Marwick, 2004 – Marwick, T.H. (2004). Use of tissue Doppler imaging to facilitate the prediction of events in patients with abnormal left ventricular function by dobutamine echocardiography. *Am J Cardiol.* 93: 142-146.

Ommen et al., 2000 – *Ommen, S.R. et al.* (2000). Clinical utility of Doppler echocardiography and tissue Doppler imaging in the estimation of left ventricular function: A comparative simultaneous Doppler-catheterization study. *Circulation.* 102: 1788-1794.

Ommen et al., 2000 – Ommen, S.R. et al. (2000). Clinical utility of Doppler echocardiography and tissue Doppler imaging in the estimation of left ventricular function: A comparative simultaneous Doppler-catheterization study. *Circulation*. 102: 1788-1794.

Otto et al., 2013 – *Otto, C. et al.* (2013). Textbook of clinical echocardiography, 5th Edition, Copyright © Saunders, 2: 61.

Otto et al., 2013a – *Otto, C. et al.* (2013). Textbook of clinical echocardiography, 5th Edition, Copyright © Saunders, 2: 61.

Rahman et al., 2011 – *Rahman, H.U. et al.* (2011). Assessment of left ventricular systolic and diastolic function by Tissue Doppler imaging after acute myocardial infarction. *Pakistan Department of Cardiology.* 23(2): 108-109.

Rahman et al., 2011 – *Rahman, H.U. et al.* (2011). Assessment of left ventricular systolic and diastolic function by Tissue Doppler imaging after acute myocardial infarction. *Pakistan Department of Cardiology.* 23(2): 108-109.

Salehi et al., 2010 – *Salehi, R. et al.* (2010). Evaluation of Systolic And Diastolic Function of Left Ventrical by using velocities of Mitral Annulus in patients with first acute Anterior Myocardial Infarction and their one month follow-up. *Journal CardiovascThorac Research.* 2(1): 9-15.

Takashioki, 2003 – Takashioki, T.Y. (2003). Diagnostic value of the atrial systolic Mitral Annular motion velocity in patients with LV systolic dysfunction. *J Am Echocardiography*. 16: 333-339.

Thygesen et al., 2012 – *Thygesen K. et al.* (2012). The Writing Group on behalf of the Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction. Third Universal Definition of Myocardial Infarction. The European Society of Cardiology, American College of Cardiology Foundation, American Heart Association, Inc., and the World Heart Federation.

Zaca et al., 2010 – *Zaca, V. et al.* (2010). Echocardiography in the assessment of left ventricular longitudinal systolic function: clinical methodology and clinical application. *Heart Fail Rev.* 15: 23-37.

Zaca, 2010 – *Zaca, V.* (2010). Echocardiography in the assessment of left ventricular longitudinal systolic function: clinical methodology and clinical application. *Heart Fail Rev.* 15: 23-37.

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Recent Advances in Colon/Colorectal Cancer Biomarker Developments

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Abstract

Cancers of the colon and rectum known as colorectal cancer. Colorectal cancer is one of the leading causes of cancer-related deaths worldwide. Colorectal cancer usually begins as a slowgrowing, non-cancerous polyp, which can progress over time to aggressive cancer. If a cancerous polyp is not removed, it can enter the lining of the large intestine, causing the cancer to spread to other organs through the blood or lymphatic vessels. With screening, it is possible to detect and remove polyps before they become cancerous. The increase in colorectal cancer awareness and screening has contributed to an overall decrease in the incidence of colorectal cancer over the past 30 years. Scientist have learned a lot about colorectal cancer, but it needs more research to find ways to prevent and detect the disease earlier. It is difficult to detect in the early stages. However, secretory proteins have been used as an ideal biomarker to detect the progression of colon cancer in cancer patients. Colorectal cancer detection techniques at the molecular level have facilitated the development of new signature drugs designed to inhibit unique pathways of colorectal cancer development and immunity.Serum/tissue protein expression may help general practitioners to identify colon cancer in earlier stages. Recently, the discovery of biomarkers is important in cancer biology and disease management. DNA, RNA, metabolites, enzymes, mRNAs, aptamers, and proteins biomolecules may help an early prediction of disease. This review explains recent advances on new developments in molecular markers associated with colorectal cancer.

Keywords: color, colorectal, cancer, biomarker, mutation.

1. Introduction

Colon (large intestine) is a long, coiled, tube like organ that extracts water from digested food. The remaining material, solid waste called feces, moves from the colon to the rectum and leaves the body through the anus. The colon is only 6 feet (1.8 m) long. This 6 feet dense muscle is divided into four parts: the ascending colon, the transverse colon, the descending colon and the sigmoid colon. Each part represents a location in a broken rectangle shape that forms the colon in the body (Bradford, 2016). Colorectal carcinoma is one of the most common cancers and leading causes of cancer-related death in the United States (Fleming et al., 2012) with a low reported incidence in India (Patil et al., 2017). Colon cancer is a malignancy that arises from the inner lining of the colon. Most of these cancers develop from colonic polyps. Early colon cancer and colon polyps mostly have no sign and symptom of illness. Full-blown colon cancer can cause occult blood in the stool, overt rectal bleeding, bowel obstruction, and weight loss. Colon cancer risk factors include a family history of it or colonic polyps and prolonged ulcerative colitis (Melissa).

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2. Results



Fig. 1. Typical picture of colon anatomy (Hoffman)

Fig. 2. Colon cancer in the cecum (Akihiro Kobayashi et al., 2006)

Biomarkers for early detection

Tumor endothelial markers (TEMs): Tumors and normal endothelium can be easily identified on the basis of TEMs. The most promising TEM1, TEM5, TEM7 and TEM8 appeared to be promising for oncogenic signaling in colorectal cancer. Over expression of TEMs, especially TEM1, TEM7, and TEM8 in colorectal tumor tissues, compared to healthy tissues, suggest their role in the formation of tumor blood vessels. These TEMs appear to be candidates for perspective for early detection, monitoring, and treatment of CRC patients (Aukasz et al., 2016).

Carcinoembryonic antigen (CEA): CEA is a cell-surface high molecular weight glycoprotein important for cell adhesion (Shiromizu et al., 2017) CEA is usually produced at birth and is present in very small amounts in healthy patients. However, it may be elevated in CRC, other types of cancer and non-fatal conditions (Shively et al., 1980).

Annexins: In humans there are subfamilies in the annexin family; A1-A11 and A13 (Nicholson et al., 2014). The sensitivity of annexin A3, A4 and A11 peptides to early stage CRC detection is reported to be higher than CEA and as such these peptides are promising biomarkers for CRC detection (Rescher et al., 2004).

Complement component C3: Complement component C3 (C3), and its fragments C3 anaphylatoxin (C3a), have been demonstrated to have over expression in fecal, serum, and histological samples from CRC patients. C3 over expression in CRC stool samples was performed in two separate studies (Bosch et al., 2017; Bosch et al., 2012).

S100 proteins: S100 is a family calcium-binding protein, consisting of 24 members divided into three groups; only intracellular regulatory functions, only extracellular functions and those with both intracellular and extracellular functions (Donato et al., 2013). The same study identified chitinase 3-like 1 (CHI3L1) protein over expression in adenomas and advanced adenomas and CRC, with over expression confirmed to be present in the serum of patient subtypes compared to controls (Fijneman et al., 2012).

Angiogenesis biomarkers: Angiogenesis, an important step in the progression of cancer, is a new blood vessel generation from the endothelial precursor, which is mediated through a group of ligands and receptors that work together (Kerbel, 2008). A group of glycoproteins, including placental growth factor (PIGF) and the VEGF family (VEGF-A, VEGF-B, VEGF-C, and VEGF-D),

act as effectors of angiogenesis (Kerbel, 2008; Ebos et al., 2008). VEGF has been reported to have a potential value as a predictor or prognosis biomarker for metastatic CRC (Gabay et al., 1999).

Inflammatory biomarkers: In patients with inflammatory bowel diseases, chronic inflammation was suggested as an important factor for CRC and increases the risk of developing CRC with prolonged duration of colitis. Another inflammatory biomarker, macrophage inhibitory cytokine 1, has been reported to be positively associated with CRC risk (Mehta et al., 2014).

Circulating tumor cells (CTCs): CTCs are primarily tumor cells derived from primary tumors or metastases circulating in peripheral blood. CTCs in colorectal cancer have epithelial origin with a defined immunophenotyping signature (CD45-, EpCAM) (Akagi et al., 2013). This promises to develop more efficient personalized therapies to eliminate cancer stem cells in CRC patients.

Circulating cell-free DNA: The discovery of circulating cell-free DNA (ccf-DNA) may open a new possibility for non-invasive analysis of tumor-derived genetic material, as it can be isolated from human body fluids (Utting et al., 2002). MSI or LOH within CCF-DNA have been investigated from plasma/sera of CRC patients as a very valuable biomarker (Lazarev et al., 2014). Various studies have reported the diagnostic / symptomatic value of mutated genes within ccf-DNA (Diehl et al., 2008).

Circulating microRNAs: miR-21 is one of the most expressed miRNAs in CRC; and miR-21 is highly secreted by cancer cells which can be measured as exosomes or free miRNAs in plasma or serum (Schetter et al., 2008). As another potential circulating microRNA, elevated serum levels of miR-92a have been reported for adenomas and CRCs (Liu et al., 2013). Significantly higher expression of miR-17-92 cluster and miR-135 was found in CRC patients compared to healthy controls (Perilli et al., 2014).

Fecal biomarkers: Because stool markers are derived directly from tumor cells, which is considered a highly specific biomarker for CRC. These fecal biomarkers include stool DNA (sDNA), which can be used for specific cancer-related genes, miRNAs, protein biomarkers as well as secreted molecules and biochemical substances for MSI, aberrant DNA methylation, or somatic mutations. Several panels of methylated genes within sDNA have been reported for different stages of CRC, *including BMP3*, *CDH1*, *CDH13*, *CRBP1*, *CXCL12*, *ESR1*, *HLTF*, *ID4*, *IRF8*, *ITGA4*, *MINT1*, *MINT31*, *NDRG4*, *P14*, *RX3*., *SFRP2*, *SLC5A8*, and *TIMP3* (Coppedè et al., 2014).

KRAS gene mutations: KRAS, a GTPase protein, is encoded by the KRAS protoonco gene, which is an early player in many biological pathways. Differential point mutations in codons 12 and 13 of exon 2, or mutations in codon 61 of exon 3, lead to constitutive activation of the RAS signaling pathway. Therefore genetic disruption of the KRAS gene is one of the essential steps in the development of many cancers, including CRC (Santini et al., 2008).

BRAF gene mutations: BRAF is a direct downstream effect or KRAS within the Ras/Raf/MAPK signaling pathway. BRAF gene mutation has been reported to be associated with CRC development and poor prognosis of patients (Fransén et al., 2004; Davies et al., 2002). Based on previous studies, BRAF gene mutation is associated with aging, female gender, proximal colon location, poor differentiation, mucous histology, infiltrating lymphocytes and advanced stage of the disease (Li et al., 2006). BRAF mutations occur more frequently in MSI-H cases of CRC (de la Chapelle, 2002).

TP53 gene mutations: The TP53 gene is a very important tumor suppressor, which plays a role as a central regulator of various cellular processes, including growth arrest and apoptosis, DNA damage, stress response, oxidative stress and prolific signals (Vogelstein et al., 2000). TP53 protein dysfunction is a common hallmark of human solid tumors, reported in more than 25 % of adenomas and CRC in 50-70 % of patients (Leslie et al., 2002).

APC/b-Catenin Mutation: Genetic disruption of APC leading to the activation of Wnt pathway, is one of the important early genetic event in genetic disruption of APC leads to activation of the Wnt pathway, an important early genetic event in colorectal tumorigenesis (Powell et al., 1992). The *APC* gene product is a large protein that regulates development, chromosomal segregation, cellular differentiation, polarity, adhesion, migration, and also apoptosis. APC promoter hypermethylation is also reported in more than 18 % of primary colorectal carcinomas and adenomas (Esteller et al., 2000).

Aberrant DNA hypermethylation in CRC: Recently a third class of CRCs characterized by a high frequency of DNA hypermethylation has been reported and defined as having a "CpG

island methylator phenotype(CIMP). A study report CIMP in CRC, based on the methylation status of five genes (*CACNA1G*, *IGF2*, *NEUROG1*, *RUNX3*, and *SOCS1*) (Weisenberger et al., 2006). These hypermethylation of various genes, i.e. *SLC5A8*, *ITGA4*, *SFRP2*, *PTCH1*, *CDKN2A*, *HLTF*, and *MGMT* play a role in the initiation and progression of adenomas to CRC (Qi et al., 2006; Li et al., 2003). To date, a large number of hypermethylated genes including *APC*, *ATM*, *BMP3*, *CDKN2A*, *SFRP2*, *GATA4*, *GSTP1*, *HLTF*, *MLH1*, *MGMT*, *NDRG4*, *RASSF2A*, *SFRP2*, *TFP12*, *VIM*, and *WIF1*, have been found in stool DNA assays for the early detection of CRC (Chen et al., 2005).

Telomere length dynamics: In mammals the ends of chromosomes are composed of telomeres, a 6-bp variable repeat sequence (TTAGGG), which is added by elomerase and plays an important role in the maintenance of chromosomal stability (Chen et., 2005; Blackburn et al., 1991). Since tumors in the sporadic form of CRC appear relatively later than hereditary nonpoliposis colorectal cancer (HNPCC), the number of splits between initiation and clinical presentation in sporadic may be higher than HNPCC, hence their baseline likely to occur upon initiation of telomere. Shortened to sporadic form of CRC (Muraki et al., 2012; Bisoffi et al., 2006). Well-differentiated tumors, suggesting a shortening of telomere length as an early event in colorectal cancer, directly reflecting pathologic cell proliferation (O'Sullivan et al., 2006; Raynaud et al., 2008).

3. Conclusion

Several biomarkers of colon/colorectal cancer have been proposed and understanding the behavior of CRC at the molecular level has been encouraged. Even if further validation studies are required, assessing the role of a biomarker in experimental models and in patients may open new perspectives regarding the patient-tailored approach. Biomarker development can target therapies for cancer and improve the selection of adjuvants for drug development. The use of protein biomarkers may also reduce economic burden in the treatment of cancer. In addition, an automated and inexpensive standardized protein marker is required for colon cancer detection. Existing colon cancer biomarker screening assays with high accuracy need to be improved. The discovery of more specific serum and tissue proteins is required in colorectal cancer patients and may enhance the development of new drugs.

References

Akagi et al., 2013 – Akagi, Y., Kinugasa, T., Adachi, Y, Shirouzu, K. (2013). Prognostic significance of isolated tumor cells in patients with colorectal cancer in recent 10-year studies. *Mol Clin Oncol.* 1: 582-592.

Bradford, 2016 – Bradford, A. (2016). Live Science Contributor. March 25. [Electronic resource]. URL: https://www.livescience.com/52026-colon-large-intestine.html

Aukasz et al.,2016 – *Aukasz, Pietrzyk* (2016). Biomarkers Discovery for Colorectal Cancer: A Review on. Tumor Endothelial Markers as Perspective Candidates. Disease Markers. 1-11.

Bisoffi et al., 2006 – *Bisoffi, M., Heaphy, C.M., Griffith, J.K.* (2006). Telomeres: prognostic markers for solid tumors. *Int J Cancer.* 119: 2255-2260.

Blackburn et al., 1991 – Blackburn, E.H. (1991). Structure and function of telomeres. *Nature*. 350: 569-573.

Bosch et al., 2012 – Bosch, L.J., De Wit, M., Oudgenoeg, G., Hiemstra, A.C., Mongera, S., Piersma, S.R. et al. (2012). Stool proteomics reveals new candidate biomarkers for colorectal cancer screening. *Gastroenterology*. 1: S524.

Bosch et al., 2017 – Bosch, L.J.W., De Wit, M., Pham, T.V., Coupe, V.M.H., Hiemstra, A.C., Piersma, S.R. et al. (2017). Novel stool-based protein biomarkers for improved colorectal cancer screening. Annals of Internal Medicine. 167(12): 855-866.

Chen et., 2005 – Chen, W.D., Han, Z.J., Skoletsky, J., Olson, J., Sah, J., Myeroff, L. et al. (2005). Detection in fecal DNA of colon cancer-specific methylation of the nonexpressed vimentin gene. J Natl Cancer Inst. 97: 1124-1132.

Coppedè et al., 2014 – Coppedè, F., Lopomo, A, Spisni, R., Migliore, L. (2014). Genetic and epigenetic biomarkers for diagnosis, prognosis and treatment of colorectal cancer. World J Gastroenterol. 20: 943-956.

Davies et al., 2002 – Davies, H., Bignell, G.R., Cox, C., Stephens, P., Edkins, S., Clegg, S, Teague, J. et al. (2002). Mutations of the BRAF gene in human cancer. Nature. 417: 949-954.

de la Chapelle., 2002 –*de la Chapelle, A., Palomaki, G., Hampel, H.* (2002). Identifying Lynch syndrome. *Int J Cancer.* 125: 1492-1493. 33. Vogelstein B., Lane D., Levine A.J. Surfing the p53 network. *Nature.* 408: 307-310.

Diehl et al., 2008 – Diehl, F., Schmidt, K., Choti, M.A., Romans, K., Goodman, S., Li, M. et al. (2008). Circulating mutant DNA to assess tumor dynamics. *Nat Med.* 14: 985-990.

Donato et al., 2013 – Donato, R., Cannon, B., Sorci, G., Riuzzi, F., Hsu, K., Weber, D.J. et al. (2013). Functions of S100 proteins. *Current Molecular Medicine*. 13(1): 24-57.

Ebos et al., 2008 – *Ebos, J.M., Lee, C.R., Bogdanovic, E., Alami, J., Van Slyke, P., Francia G. et al.* (2008). Vascular endothelial growth factor-mediated decrease in plasma soluble vascular endothelial growth factor receptor-2 levels as a surrogate biomarker for tumor growth. *Cancer Res.* 68: 521-529.

Esteller et al., 2000 – Esteller, M., Sparks, A., Toyota, M., Sanchez-Cespedes, M., Capella, G., Peinado, M.A. et al. (2000). Analysis of adenomatous polyposis coli promoter hypermethylation in human cancer. Cancer Res. 60: 4366-4371.

Fijneman et al., 2012 – Fijneman, R.J.A., De Wit, M., Pourghiasian, M., Piersma, S.R., Pham, T.V., Warmoes, M.O. et al. (2012). Proximal fluid proteome profiling of mouse colon tumors reveals biomarkers for early diagnosis of human colorectal cancer. *Clinical Cancer Research*. 18(9): 2613-2624.

Fransén et al., 2004 – Fransén, K., Klintenäs, M., Osterström, A., Dimberg, J., Monstein, H.J., Söderkvist, P. (2004). Mutation analysis of the BRAF, ARAF and RAF-1 genes in human colorectal adenocarcinomas. *Carcinogenesis.* 25: 527-533.

Gabay et al., 1999 – *Gabay, C., Kushner, I.* (1999). Acute-phase proteins and other systemic responses to inflammation. *N Engl J Med.* 340: 448-454.

Kerbel, 2008 – Kerbel, R.S. (2008). Tumor angiogenesis. N Engl J Med. 358: 2039-2049.

Akihiro Kobayashi et al., 2006 – *Akihiro Kobayashi, Norio Saito, Yasushi Sano, Shigeharu Kato, Hiroaki Ikematsu, Takahiro Fujimori et al.* (2006). Alpha-fetoprotein-producing colon cancer with atypical bulky lymph node metastasis. *World J Gastroenterol.* 12(47): 7715-7716.

Lazarev et al., 2014 – Lazarev, I., Leibovitch, L., Czeiger, D., Sion-Vardi, N., Geffen, D.B., Douvdevani, A., Ariad, S. (2014). Cell-free DNA blood levels in colorectal cancer patients do not correlate with mismatch repair-proficiency. *In Vivo.* 28: 349-354.

Leslie et al., 2002 – *Leslie, A., Carey, F.A., Pratt, N.R., Steele, R.J.* (2002). The colorectal adenomacarcinoma sequence. *Br J Surg.* 89: 845-860.

Li et al., 2003 – *Li*, *H.*, *Myeroff*, *L.*, *Smiraglia*, *D.*, *Romero*, *M.F.*, *Pretlow*, *T.P.*, *Kasturi*, *L. et al.* (2003). SLC5A8, a sodium transporter, is a tumor suppressor gene silenced by methylation in human colon aberrant crypt foci and cancers. *Proc Natl Acad Sci USA*. 100: 8412-8417.

Li et al., 2006 – *Li, W.Q., Kawakami, K., Ruszkiewicz, A., Bennett, G., Moore, J., Iacopetta, B.* (2006). BRAF mutations are associated with distinctive clinical, pathological and molecular features of colorectal cancer independently of microsatellite instability status. *Mol Cancer.* 5: 2.

Liu et al., 2013 – Liu, G.H., Zhou, Z.G., Chen, R., Wang, M.J., Zhou, B., Li, Y., Sun, X.F. (2013). Serum miR-21 and miR-92a as biomarkers in the diagnosis and prognosis of colorectal cancer. *Tumour Biol.* 34: 2175-2181.

Fleming et al., 2012 – *Fleming M., Ravula S., Tatishchev S.F., Wang H.L.* (2012). Colorectal carcinoma: Pathologic aspects. *J Gastrointest Oncol.* 3(3): 153-17.

Hoffman – Hoffman, M. Human Anatomy. [Electronic resource]. URL: https://www.webmd.com/digestive-disorders/picture-of-the-colon#1

Mehta et al., 2014 – *Mehta, R.S., Song, M., Bezawada, N., Wu, K, Garcia-Albeniz X., Morikawa T. et al.* (2014). A prospective study of macrophage inhibitory cytokine-1 (MIC-1/GDF15) and risk of colorectal cancer. *J Natl Cancer Inst.* 106: dju016.

Melissa-Melissa... – Melissa-Melissa Conrad Stöppler, Colon Cancer. [Electronic resource]. URL: https://www.medicinenet.com/colon_cancer/article.htm

Muraki et al., 2012 – *Muraki, K., Nyhan, K., Han, L., Murnane, J.P.* (2012). Mechanisms of telomere loss and their consequences for chromosome instability. *Front Oncol.* 2: 135.

Nicholson et al., 2014 – Nicholson, B.D., Shinkins, B., Pathiraja, I., Roberts, N.W., James, T.J., Mallett, S. et al. (2014). Blood CEA levels for detecting recurrent colorectal cancer (protocol). Cochrane Database of Systematic Reviews. 12:6.

O'Sullivan et al., 2006 – O'Sullivan, J., Risques, R.A., Mandelson, M.T., Chen, L., Brentnall, T.A., Bronner, M.P. et. al. (2006). Telomere length in the colon declines with age: a relation to colorectal cancer? *Cancer Epidemiol Biomarkers Prev.* 15: 573-577.

Patil et al., 2017 – Patil, P.S., Saklani, A., Gambhire, P., Mehta, S., Engineer, R., De'Souza, A. et al. (2017). Colorectal Cancer in India: An Audit from a Tertiary Center in a Low Prevalence Area. Indian J Surg Oncol. 8(4): 484-490.

Perilli et al., 2014 – Perilli, L., Vicentini, C., Agostini, M., Pizzini, S., Pizzi, M., D'Angelo, E., Bortoluzzi, S., Mandruzzato, S., Mammano, E., Rugge, M., Nitti, D., Scarpa, A., Fassan, M., Zanovello, P. (2014). Circulating miR-182 is a biomarker of colorectal adenocarcinoma progression. Oncotarget. 5: 6611-6619.

Powell et al., 1992 – Powell, S.M., Zilz, N., Beazer-Barclay, Y., Bryan, T.M., Hamilton, S.R., Thibodeau, S.N., Vogelstein, B., Kinzler, K.W. (1992). APC mutations occur early during colorectal tumorigenesis. Nature. 359: 235-237.

Qi et al., 2006 – Qi, J., Zhu, Y.Q., Luo, J, Tao, W.H. (2006). Hypermethylation and expression regulation of secreted frizzled-related protein genes in colorectal tumor. *World J Gastroenterol*. 12: 7113-7117.

Raynaud et al., 2008 – Raynaud, C.M., Jang, S.J., Nuciforo, P., Lantuejoul, S., Brambilla, E., Mounier, N. et.al. (2008). Telomere shortening is correlated with the DNA damage response and telomeric protein down-regulation in colorectal preneoplastic lesions. Ann Oncol. 19: 1875-1881.

Rescher et al., 2004 – *Rescher, U., Gerke, V.* (2004). Annexins – Unique membrane binding proteins with diverse functions. *Journal of Cell Science*. 117: 2631-2639.

Santini et al., 2008 – Santini, D., Loupakis, F., Vincenzi, B., Floriani, I., Stasi, I., Canestrari, *E*, *Rulli*, *E*. *et al.* (2008). High concordance of KRAS status between primary colorectal tumors and related metastatic sites: implications for clinical practice. Oncologist. 13: 1270-1275.

Schetter et al., 2008 – Schetter, A.J., Leung, S.Y., Sohn, J.J., Zanetti, K.A., Bowman, E.D., Yanaihara, N., Yuen, S.T., Chan, T.L., Kwong, D.L, Au, G.K., Liu, C.G., Calin, G.A., Croce, C.M., Harris, C.C. (2008). MicroRNA expression profiles associated with prognosis and therapeutic outcome in colon adenocarcinoma. JAMA. 299: 425-436.

Shiromizu et al., 2017 – Shiromizu, T., Jume, H., Ishida, M., Adachi, J., Kano, M., Matsubra, H., et al. (2017). Quantitation of putative colorectal cancer biomarker candidates in serum extracellular vesicles by targeted proteomics. *Scientific Reports*. 7: 12782.

Shively et al.,1980 – *Shively, J.E., Todd, C.W.* (1980). Carcinoembryonic antigen A: Chemistry and biology. Cancer Markers. *Contemporary Biomedicine*. 1: 295-314.

Utting et al., 2002 – Utting, M., Werner, W., Dahse, R., Schubert, J., Junker, K. (2002). Microsatellite analysis of free tumor DNA in urine, serum, and plasma of patients: a minimally invasive method for the detection of bladder cancer. *Clin Cancer Res.* 8: 35-40.

Vogelstein et al., 2000 – Vogelstein, B., Lane, D., Levine, A.J. (2000). Surfing the p53 network. Nature. 408: 307-310.

Weisenberger et al., 2006 – Weisenberger, D.J., Siegmund, K.D., Campan, M., Young, J., Long, T.I., Faasse, M.A. et al. (2006). CpG island methylator phenotype underlies sporadic microsatellite instability and is tightly associated with BRAF mutation in colorectal cancer. Nat Genet. 38: 787-793.

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Co-morbidities of Microcytic Anemia in Severe Acute Malnutrition Infants: A Tertiary Care Hospital Experience in Central India

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Abstract

When microcytosis occur with severe acute malnutrition it is characterized by body's tissues thus organs do not get enough oxygen as the red blood cells becomes smaller in size and carries less oxygen which causes sudden major weight loss requiring a quick nutritional and medical intervention. SAM was diagnosed by WHO – MUAC method. Complete blood count and red cell indices were measured by automated 5-part hematoanalyzer and microcytosis was determined by peripheral smear method.Among all SAM infants with microcytic anemia; WBC was elevated and comparative mean value of RBC, MCV and MCH were statistically significant. Xeropthalmic stage and eyes puffiness was associated clinical symptoms of SAM infants with microcytosis. The result of the study emphasizes the importance of identifying the co-morbidities of microcytic anemia in SAM infants.

Keywords: malnutrition, microcytosis, anemia, sam.

1. Introduction

Malnutrition is a common problem in developing countries and often associated with comorbidities (Thapa et al., 2015). Globally, more than one- third of under-five deaths are attributed to under nutrition and of these, 10 % are severely malnourished (UNICEF-WHO, 2013; Collins et al., 2006). Severe acute malnutrition, among children below five years of age remains a major embarrassment and impediment to optimal human capital development in India (Vaid et al., 2018). Anemia is usually classified based on the size of RBCs, as measured by the mean corpuscular volume (MCV). Anemia can be microcytic (MCV typically less than 80 fL), normocytic (80 to 100 fL), or macrocytic (greater than 100 fL). The RBC distribution width is a measure of the size variance of RBCs. A low RBC distribution width suggests uniform cell size, whereas an elevated width (greater than 14 percent) indicates RBCs of multiple sizes. Anemia impairs normal development, decreases physical exercise tolerance & intellectual performance in children which may lead to a slowdown of growth in children. It constitutes a major public health problem in young children in the developing world with wide social & economic implications (Ouaderi et al., 2016). Causes of anemia in the newborn are blood loss, decreased RBC production, and increased RBC turnover. Blood loss during delivery can result from a ruptured umbilical cord, placenta previa, and abruptio placentae. Maternal-fetal transfusion occurs in 50 % of all pregnancies, but usually does not cause significant loss of blood volume. The patient's history eliminates most of these causes. Anemia is commonly associated with nutritional deficiencies such as iron deficiency, the main factor responsible for microcytic anemia, while folate or vitamin B12 deficiencies are

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responsible for macrocytic anemia (Dallman et al., 1980; Fleming et al., 1982). It results in the various pathophysiological changes in the body systems including significant changes in hematological parameters. Low red cell counts resulting in anemia has always been a constant feature of protein energy malnutrition and may be normochromic normocytic, microcytic hypochromic or macrocytic anemia (Lukens et al., 1995; Warrier et al., 1990). Anemia associated with severe malnutrition is the consequence of multiple factors and represents an interaction between adaptation to inadequate food intake and the impact of other stresses associated with infection or dietary imbalance (Kraemer et al., 2007). There is none of the reported literature available with details of co-morbidities with microcytic anemia associated with severe acute malnourished children. Thus the aim of this study was to determine the pathophysiological co-morbidities of microcytosis in SAM infants.

2. Materials and methods

Study subjects were severe acute malnutrition children; admitted in SAM unit, Department of Paediatrics, Gandhi memorial hospital Rewa, Madhya Pradesh. Study was approved by the institutional ethical committee. Malnourished children were screened as per WHO Mid-upper arm circumference (MUAC) under nutrition guidelines. About 2 ml venus blood was collected after taking signed consent from children parents. Complete blood count and red cell indices were measured by automated 5-part hematoanalyzer (SYSMEX XS-800i, Kobe Japan) using Transasia diagnostic kit. Leishman stain was used in peripheral smear for determination of red cell size in binocular microscope (Olympus CX21ILED). Unpaired *t*-test was used to compare the mean calculated of two groups on GraphPad (version 3.06) software. The *P* value < 0.05 was considered statistically significant.

3. Results

This cross-sectional study was conducted in Multidisciplinary Research Unit, Shyam Shah Medical College, Rewa, Madhya Pradesh over a period of one year from January 2018 to December 2018. A total 74 clinically symptomatic severe acute malnourished infants blood samples were collected and categorised in two groups. First group had 42 SAM infants with microcytosis (22 male and 20 female with mean age 13.23 \pm 7.02 months) while second group had 32 SAM infants without microcytosis included 26 normocytic and 6 macrocytic anaemia (15 male and 17 female with mean age 15.62 \pm 9.68 months). Haematological profile of SAM microcytic infants group as well as SAM without microcytosis was recorded. All the parameters were statistically significant except WBC and HGB. RBC, MCV and MCH were extremely significant. Details of the comparative value are given in Table 1. Various clinical features associated with severe acute malnutrition were documented for both groups. Hair pigmentation (100 %) was the main similar clinical finding in both groups while oedema (50 %) was presented by SAM infants without microcytosis. Xeropthalmic stage (14.2 %) and puffiness over eyes were predominated in SAM infants with microcytosis group. Detail clinical profile are depicted in Figure 1.

Haematological Profile	SAM with Microcytosis (N=42) Mean±SD	SAM without Microcy (N=32)	tosis <i>P</i> value
WBC(ths/ul)	12 44+6 33	10 10+5 10	0 106
RBC (millions/ µl)	4.16 ± 0.867	2.89±1.21	< 0.001
HGB(g/dl)	8.33 ± 1.810	74±2.33	0.224
MCV(fl)	67.37±8.158	93.73 ± 11.25	< 0.001
MCH(pg)	20.33 ± 3.88	29.01± 7.85	< 0.001
MCHC(g/dl)	28.57 ± 3.713	30.79±5.46	0.076
PLT(ths/µl)	2.88 ± 1.55	2.25 ± 1.68	0.099

Table 1. Hematological profile of SAM infants



Fig. 1. Comparative clinical frequency (%) of SAM with microcytosis and without microcytosis

4. Discussion

Child malnutrition is a major global health problem contributing to childhood morbidity, mortality, impaired intellectual development, suboptimal adult work capacity and increased risk of diseases in adulthood. The mortality rate of children with complicated severe acute malnutrition in hospitalized set-up also remains high (Collins et al., 2006). Also high mortality has been attributed to co-morbidities like infections and associated complications. The most common type of anemia was microcytic followed by megaloblastic anemia reported in a study of Kangra district Himanchal Pradesh (Vaid et al., 2018). Anemia being very common in childhood; more seen in aged 6 months to 24 months old. When discussed about its prevalence in SAARC in Bangladesh 68 % of children aged 6-59 months are anemic also in third world countries, 39 % children below 5 years and 48 % children between 5–14 years are suffering from anemia. Children with anemia may present in hospital with anemia related nonspecific or specific symptoms or with other associated diseases (Ghosh et al., 2015). We report the elevation of WBC in SAM with microcytosis; however it was not statistically significant (P value 0.106) which showed the patients are prone to infection. Mean value of RBC (*P* value < 0.001), MCV(*P* value < 0.001) and MCH (*P* value < 0.001) were showed extremely significant in compared groups. Mean value of MCHC (P value 0.076) and Platelet (P value 0.099) was significant in compared groups. Similar finding was reported in previous studies (Saka et al., 2012; Laditan et al., 1983; El-Nawawy et al., 2002). It is reported that, in Asia, the prevalence of anemia in children below two years of age will possibly surpass 90 % of children if not addressed as important health issues (Janus et al., 2010). The prevalence of anemia in India was reported 74.35 % for 6-35 months age group & neighbor country Nepal has 78 % anemic cases for 6-59 months age group. Going towards east Kazakhstain reported 73.7 % anemic cases for 0-23 months age group. The prevalence of anemia in preschool children (0-4 yr) of Africa, southeast Asia and eastern Mediterranean were 67.6 %, 65.5 % and 46.7 % cases were reported respectively. The prevalence of anemia in developed countries i.e. in America 29.3 % and Europe 21.7 % cases were reported (Benoist et al., 2008). In our study; cases of SAM with microcytic anemia was highly associated with xeropthalmic stage and eyes puffiness while oedema and lymphadenopathy was significantly high in SAM without microcytosis. A study reported microcytosis in control group 40.6 % and macrocytosis 33 % in SAM children (Dwivedi et al., 2017). Other studies reported acute gastroenteritis being the most common co-morbid condition on followed by respiratory tract infections in their cohort of SAM (Talbert et al., 2012; Kumar et al., **2014**; **Sunguya** et al., **2006**; **Irena** et al., **2011**). With detailed discussion it appears that malnutrition is still a common problem in developing countries.

5. Conclusion

Hospitalized SAM infants were found associated with co-morbidities of microcytic anemia. Among all SAM infants with microcytic anemia; WBC was elevated and comparative mean value of RBC, MCV and MCH were statistically significant. Xeropthalmic stage and eyes puffiness is associated clinical symptom of SAM infants with microcytosis. These results emphasize the importance of identifying the co-morbidities of microcytic anemia in SAM infants.

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References

Benoist et al., 2008 – Benoist, B., McLean, E., Egli, I, Cogswell, M. (2008). Worldwide prevalence of anemia 1993-2005: WHO Global Database on Anemia. Geneva: World Health Organization.

Collins et al.,2006 – *Collins, S, Dent, N, Binns, P, Bahwere, P, Sadler, K, Hallam, A*. (2006). Management of severe acute malnutrition in children. *Lancet*. 368: 1992-2000.

Dallman et al., 1980 – Dallman, P.R., Siimes, M.A., Stekel, A. (1980). Iron deficiency in infancy and childhood. *Am J Clin Nutr*. 33: 86-18.

Dwivedi et al., 2017 – Dwivedi, D, Singh, V, Singh, J, Sharma, S. (2017). Study of Anaemia in Children with Severe Acute Malnutrition. J Nepal Paediatr Soc. 37(3): 250-253.

El-Nawawy et al., 2002 – *El-Nawawy, S., Barakat, T., Elwalily, A., Deghady, A.M., Hussein, M.* (2002). Evaluation of erythropoiesis in Protein Energy Malnutrition. *East. Med Health J.* 8: 2-3.

Fleming et al.,1982 – *Fleming, A.F., Werblinska, B.* (1982). Anemia in childhood in the guinea savana of Nigeria. *Ann Trop Paediatr.* 2: 161-73.

Ghosh et al., 2015 – Ghosh, A., Ghartimagar, D., Thapa, S, Sathian, B., Asis, D. (2015). Microcytic Hypochromic Anemia in Pediatric Age Group: A Hospital Based Study in Nepal. *American Journal of Public Health Research*. 3(4A): 57-61.

Irena et al., 2011 – Irena, A.H., Mwambazi, M., Mulenga, V. (2011). Diarrhea is a major killer of children with severe acute malnutrition admitted to inpatient set-up in Lusaka, Zambia. *Nutr. J.* 10: 110.

Janus et al., 2010 – *Janus, J., Moerschel, S.K.* (2010). Evaluation of Anemia in Children. *Am Fam Physician.* 81(12): 1462-1471.

Kraemer et al., 2007 – *Kraemer, K., Zimmermann, M.B.* (2007). Nutritional anemia. Sight and life pres: 228.

Kumar et al., 2014 – *Kumar, R., Singh, J, Joshi, K, Singh, H.P., Bijesh, S.* (2014). Co morbidities in hospitalized children with severe acute malnutrition. *Indian Pediatr.* 51: 125-27.

Laditan et al., 1983 – Laditan, A.A.O., Tindimebwa, G. (1983). The Protein Energy Malnourished Child in a Nigerian Teaching Hospital. J Trop Pediatr. 29: 61-4.

Lukens et al., 1995 – *Lukens, J.N.* (1995). Iron metabolism and iron deficiency. In: Miller DR, Bodner RL, Miller LP, eds. Blood diseases of infancy and childhood. Philadelphia: Mosby: 193-219.

Quaderi et al., 2016 – *Quaderi, H.R., Hoque, M., Ahmed, N., Begum, D., Debnath, B.* (2016). Prevalence of Anemia in Children Aged Six Months to Thirty Six Months – A Hospital Based Study. *Bangladesh J Child Health.* 40(2): 98-102.

Saka et al.,2012 – Saka, A.O., Saka, M.J., Ojuawo, A., Abdulkarim, A., Bilamin, S., Latubosun, L. (2012). Haematological profile in children with protein energy malnutrition in North Central Nigeria. *Glob J Med Res.* 12(4): 1-7.

Sunguya et al., 2006 – Sunguya, B.F.P., Koola, J.I., Atkinson, S. (2006). Infections associated with severe malnutrition on among hospitalised children in East Africa. *Tanzan Health Res Bull.* 8(3): 189-92.

Talbert et al., 2012 – *Talbert A., Thuo, N., Karisa, J., Chesaro, C., Ohuma, E., Ignas, J. et al.* (2012). Diarrhoea complicating severe acute malnutriti on in Kenyan children: A prospective descriptive study of risk factors and outcome. *PLoS One.* 7: 1.

Thapa et al., 2015 – *Thapa, A., Shah, G.S., Mishra, O.P.* (2015). Analysis of Comorbidities in Children with Severe Acute Malnutrition in Eastern Nepal. *J Nepal Paediatr Soc.* 35(2): 99-102.

UNICEF-WHO, 2013 – Child Nutrition – UNICEF statistics. UNICEF-WHO world bank child Malnutrition. [Electronic resource]. URL: http://data.unicef.org/nutrition/malnutrition.html2013

Vaid et al., 2018 – Vaid, A., Sharma, M., Jamunashree, B., Gautam, P. (2018). Serum vitamin B12 levels in severe acute malnutrition hospitalized children between age group 6 months to 59 months in Kangra, India. Int J Contemp Pediatr. 5(5): 1997-2001.

Warrier et al., 1990 – *Warrier, R.P.* (1990). The anaemia of malnutrition. In: Suskind RM, Suskind LL, eds. The malnourished child. New York: Lippincott-Raven. 19: 61-72.

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The Concept of Preparing Female Students for Pregnancy Management

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Abstract

In this article topical issues addresses, related to the preparation of pregnant students for pregnancy and the birth of healthy children. The special section «Physical Education for Pregnant Women» is developed and presented in the academic discipline «Physical Education» as «Additional Type of Education» intended for students studying in non-sports specialties in higher educational establishments.

In most cases, in the process of life, all students are faced with the issues of motherhood and fatherhood, bearing healthy children and maintaining the correct lifestyle (lifestyle) during pregnancy. Surprising is the fact that these issues are not discussed in high school at school, they are not considered at the university, and only when a woman is already pregnant, she can attend theoretical classes in medical institutions, practical classes in various health and fitness centers (on a paid basis) or be self-taught and study the necessary material on your own.

In our opinion, it is necessary to approach this period in life more consciously, to prepare your body in advance for bearing and giving birth to a healthy child. Be prepared for physiological changes and hormonal changes that will ensure the correct development of the fetus, as well as prepare for the upcoming delivery.

If a woman in advance will think more seriously about her health and prepare her body for conception, then in the future we will be able to prevent the appearance of many problems and thus get away from the phrase – «A sick child is born from unhealthy parents».

Keywords: higher educational establishments, physical education, students, trimesters of pregnancy, physiological changes, health, the curriculum, exercise.

1. Introduction

Nowadays, maintaining and strengthening the health of pregnant women is the main vector of the State policy of the Republic of Belarus. According to official figures in our country more than 73 % of women in pregnancy have disabilities, which are reflected in the childbearing function, and in the future also in the state of health of children.

The health of pregnant women, as well as the category of women who are trained in higher educational establishments with the status of «student», deserves close attention, because they fulfill the main task – the birth of healthy children, which means a healthy nation, the future of our state. According to analytical data, the number of pregnant students studying at higher educational establishments increases annually.

The current situation shows that modern youth often lack the main values in life, the socalled new lifestyle has been formed, with accompanying chronic and acquired diseases and bad habits that negatively affects the general health of female students.

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Given the above, we have come to the conclusion that the best response to adverse factors is regular physical education, which in turn helps restore, strengthen and preserve the health of pregnant students.

The purpose of the work is a theoretical and experimental justification for organizing classes in the educational discipline «Physical Education» for pregnant students studying at a higher educational establishment.

2. Materials and methods

The research was carried out on the basis of the educational institution «Vitebsk State University named after P.M. Masherov», which was attended by 25 female students studying at the KhGF, BF, FMiIT and IF, aged 20 to 23 years. These students did not have deviations in health and belonged to the main educational department before pregnancy.

Specific pedagogical methods were used as research methods. Namely theoretical and empirical.

3. Results

Nowadays, there is no higher educational establishment in the Republic of Belarus which provides for the training of pregnant students for the upcoming birth. Mainly, pregnancy is carried out by doctors, who often take necessary tests and prescribe a certain list of medicines and vitamins. There are pre-pregnancy rooms that do not reflect a complete picture of the course of pregnancy and the outcome of childbirth in individual women's clinics.

Currently, pregnant students, studying at a higher educational establishment in non-sports specialties have a choice: to undergo a course of special training for childbirth in medical institutions or private fitness organizations. But the specifics of this training have not been improved enough, because women's consultations at clinics, in schools for pregnant women, only theoretical classes are held in the amount of 4 hours monthly, without practical material. In private sports and recreation organizations, practical classes are held in an amount of 2 times a week for a duration of 30 minutes, only for persons who do not have a deviation in their state of health and associated chronic diseases. Classes are practical and conducted on a paid basis.

Today, there are no pregnancy programs specially designed for each woman (student) for nine months, taking into account individual characteristics, chronic diseases, professional activities and age.

We analyzed the work of the UVO in the educational discipline «Physical Culture», studied regulatory documents, analyzed the activities of medical institutions and private fitness organizations for pregnant women. In that way, we approached the question: why UVO can train good specialists, open new specialties, provide practical bases where students can consolidate their knowledge. But unfortunately, UVO does not provide for the preparation of pregnant students in the educational discipline «Physical Education» for the informed correct management of pregnancy, the birth of healthy children and the care of newborns. It turns out that one of the important stages in any woman's life is fixed at the level of instinct. Which in our view is a crucial moment in the life of any woman.

Working in the educational system in the field of physical education, we were looking for ways to solve this issue. Studying opinions of a number of scientists (Balsevich, 2005; Lubysheva, 2004; Stolyarov, 2012), we found out that the modern system of this pedagogical activity is not effective enough and needs modernization. Almost in all countries there is critical position of modern physical education, especially in educational establishments. The view is expressed that many physical educational curriculum are in deep crisis (Hardman, 2011).

In this regard, the problem of modernizing the modern system of physical education is urgent.

Yu.M. Nikolaev (2012) argued that – «We have come to the milestone when the choice of a strategy for the development of physical culture and physical education is important. And this choice will depend on the real progress in these critical areas of society and the individual, in general, the prestige of the sphere of physical culture» (Nikolaev, 2012).

The educational discipline «Physical Culture» in a higher education institution should reflect activities in the field of quality policy of general physical education, namely: update the content of the discipline, improve the effectiveness of physical education teaching in the context of the implementation of the program for the health saving of students, use individual approaches in training and the formation of vocational competencies of a graduate (Koleda, 2017).

The purpose of the «Physical Culture» discipline in higher education is to develop the social and personal competencies of students, ensuring the targeted use of appropriate means of physical culture and sports for the preservation, promotion of health and preparation for professional activity.

Since human life and health are the main values, education is subordinate to the idea of enriching these values (Polyakova, 2012).

4. Discussion

In view of the above, there is a need to improve the educational process in the educational discipline «Physical Culture» in the institution of higher education and to create all conditions for the successful course of pregnancy, childbirth, the birth of healthy children and the care of newborns. The solution to this issue lies in the introduction of an innovative form of organizing classes in the educational discipline «Physical culture» for students with various trimesters of pregnancy, studying in non-sports specialties as «Additional type of training» under the special section «Physical culture during pregnancy». This innovation allows you to prepare the body of the future mother for childbirth, and get the necessary level of theoretical knowledge.

The introduction of the specially developed section «Physical culture during pregnancy» for pregnant students was carried out on the basis of the educational institution «Vitebsk State University named after P.M. Masherov» in the period from 2015 to 2018.

Offering an innovative form of organizing classes for pregnant students studying at a higher education institution should first of all take into account the main changes that occur in the body of students during pregnancy.

With the onset of pregnancy in the body of female students, certain changes occur in the body systems, such as: cardiovascular, respiratory, nervous, hormonal, digestive, musculoskeletal system.

Let's take a closer look at the changes in the presented systems.

In the cardiovascular system, an increase in vascular tone is noted, due to which, by the end of pregnancy, a pulse increase of approximately 10 beats per minute. The minute volume of blood also changes with a gradual increase to a maximum by the 25th-32nd week, and then it remains at a high level and decreases before childbirth. By the end of pregnancy, the increase in minute volume is about 40-45 %. The total mass of circulating blood also increases. This is due to the development of utero-placental circulation. Late toxicosis of pregnant women may also be associated with dilation of the venous knee in capillaries, resulting in slowing blood flow.

In the respiratory system, changes occur from the first weeks of pregnancy. The minute volume of breathing increases and remains at a fairly high level. The frequency of breathing does not change. Before childbirth, the diaphragm rises by 4 cm. Changes in the thorax occur. The vertical size of the chest decreases, but its circumference increases. There are no significant changes in the life capacity of lungs.

In the nervous system, cyclic changes in nervous processes occur. In the first trimester of pregnancy, excitation processes dominate, which from the middle of the second trimester are replaced by inhibition. 75 % of pregnant students have psychoemotional changes. At the beginning of pregnancy, the taste changes, drowsiness, plaquity and irritability appear. At the end of pregnancy, a depressive state appears, turning into anxiety for the outcome of childbirth.

The hormone system is also subject to changes. Sex hormones progesterone and estrogen increase approximately 100-fold. The function of the endocrine glands also changes. The thyroid gland also increases.

In the digestive system, pressure in the abdomen mainly increases. The functioning of the liver, which synthesizes a large amount of protein, is enhanced. With an increase in the fetus, the stomach acquires a horizontal position. Heartburn appears.

The musculoskeletal system is subject to changes, which is reflected in the softening of the ligament apparatus of the pelvic joints. The placenta and yellow body release the hormone relaxin, which increases the stretchability of the ligaments (pubic symphysis, sacroiliac and coccyx joints). Physiological expansion of pubic symphysis is within 1.5-7 mm. In addition, it loosens, thereby increasing mobility. After childbirth, this process is characterized by reverse development. With an

increase in fetal weight and body weight of the pregnant woman, a shift in the general center of gravity occurs, lumbar lordosis increases.

The main part of the classes uses special exercises. In the preparatory and final parts general developmental exercises are used. Classes must be held 3 times a week. In a well-ventilated room with an air temperature about 18–20 °C. During the visit of classes, pregnant female students should wear loose clothing that does not restrict movement. The duration of classes initially increases from 15 to 40 minutes, and then in the third trimester should be no more than 25 minutes. On the lessons, it is necessary to use a differentiated approach to the dosage of physical activity and the nature of the exercises used. The differentiated approach is used taking into account the physical fitness of pregnant female students. Special care must be taken during the first trimester of pregnancy, on the days of menstruation and at the end of the third trimester of pregnancy. The size of the group can be from 8 to 12 people. It is advisable to conduct special classes with musical accompaniment. On the, exercises are used both with objects, and without them. You can use different starting positions, but preferably – lying on your back, on your side, standing on all fours (Venskovich, 2015).

In the first trimester of pregnancy, physical culture has a general health-improving effect on the body of students, the skills of correct diaphragmatic breathing are mastered. Gradually the cardiovascular system adapts to physical activity. Taking into account increased excitability of CNS simple exercises are used that cover large muscle groups. Exercises are performed are performed at a slow and medium pace. Students in the first trimester of pregnancy master the relaxation technique. Relaxation exercises are performed from a starting position, lying on the left side. It is considered that this position improves the relaxation of the muscles of the lower back and small pelvis (Venskovich, 2015).

In the second trimester of pregnancy, an intensive increase in the body weight of a pregnant student takes place, the general center of body weight shifts, and the location of the fundus of the uterus changes. The fundus of the uterus is at the level of the navel. In the second half of this trimester, due to a strong increase in the uterus (the bottom of the uterus is located between the xiphoid process and the navel), the mobility of the diaphragm is significantly limited, blood and lymph circulation is hampered, which is accompanied by edema of the lower extremities. There is a risk of varicose veins. Pain in the lumbar region may appear (Venskovich, 2015).

In the second trimester of pregnancy, physical education helps to strengthen the abdominal muscles, strengthen the muscles of the perineum and make them more elastic, increase the mobility of the spine, sacroiliac joints. In this period, breathing exercises are introduced with holding the breath while inhaling. It is not recommended to use the exercises in the initial prone position. Exercises for the first trimester of pregnancy are also used. Exercises are used to reduce back pain. In this way, after childbirth, well-developed muscles contract faster and prevent sagging of the abdomen and prolapse of the abdominal organs. All kinds of tilts and turns of the body, alternate flexion and extension of the lower extremities are used. Exercises for tension and relaxation of the gluteal muscles are used while the anus is pulled in. The implementation of such exercises is aimed primarily at facilitating the labor act. Exercises are used in a standing position on all fours, knee-elbow stand – abduction and adduction of straight and bent legs, flexion and extension, arching and arching of the back, lunges, half-squats with one leg resting on a gymnastic wall. Much attention is paid to corrective exercises for the feet, for the prevention of flat feet. Rides of a gymnastic stick, raising and lowering small objects from the initial sitting position are used. In the second half of this trimester, to combat edema, 50 % of the exercises are performed from the starting position, lying or sitting with the lower limbs raised. They use flexion and extension of the feet, alternately pulling the knees to the stomach (Venskovich, 2015).

In the third trimester of pregnancy, the use of physical culture helps to eliminate congestion in the small pelvis and lower extremities. Thanks to this, the achieved level of physical activity is maintained, the motor skills necessary for childbirth are developed. At this time, further difficulties in the function of external respiration, blood circulation, digestion, and venous congestion are noted. The fundus of the uterus is located at the costal arch, the range of motion in the joints of the lower extremities is limited. By the end of the third trimester, the uterus descends, facilitating the activity of the cardiovascular and respiratory systems. 90 % of physical exercises should be used from a sitting and lying position. 4 weeks before giving birth, students learn to push correctly: lying on their backs, knees bent, hands on knees, chin lowered to chest. When performing this exercise, you must take a deep breath, hold your breath and push as with a hard chair. Skills in this exercise will make the pushing activity easier. In this way, having fulfilled all the recommendations, pregnant female students successfully prepare themselves for the upcoming birth (Venskovich, 2015).

5. Conclusion

Considering the above, we have come to the conclusion that in most cases, in the process of life, all students are faced with the issues of motherhood and fatherhood, bearing healthy children and maintaining the correct lifestyle (way of life) during pregnancy. Surprising is the fact that these issues are not discussed in high school at school, they are not considered at the university, and only when woman is already pregnant, she can attend theoretical classes in medical institutions, practical classes in various health and fitness centers (on a paid basis) or be self-taught and study the necessary material on your own.

Having conducted pedagogical research for a rather long period of time, we came to the conclusion that the special section «Physical culture during pregnancy» developed earlier by us is insufficient and requires further improvement.

In our opinion, it is necessary to approach this period in life more consciously, to prepare in advance the organism of students for bearing and giving birth to a healthy child. To prepare female students for physiological changes and hormonal changes, which will ensure the correct development of the fetus, as well as preparation for the upcoming delivery.

If a woman in advance will think more seriously about her health and prepare her body for conception, then in the future we will be able to prevent the appearance of many problems and in this way get away from the phrase – «A sick child is born from unhealthy parents».

Therefore, preparation for pregnancy is not only a mass of examinations and the appointment of vitamins. It is also an understanding of the importance of all the processes that take place at the time of conception and bearing a child.

References

Balsevich, 2005 – Balsevich, V.K. (2005). Physical culture: youth and modernity. *Theory and practice of physical cultures*. 4: 2-4.

Hardman, 2011 – *Hardman, K.* (2011). Physical education in Europe. Physical education and sport education in the European Union. Pp. 3-14.

Koleda, 2017 – *Koleda, V.A.* (2017). Physical culture: typical textbook. Program for higher education Textbook. Institutions. Minsk: RIVSH. 35 p.

Lubysheva, 2004 – Lubysheva, L.I. (2004). Values of physical culture in a healthy lifestyle. Modern research in the field of sports science: materials of the international. Conf., 10–12 oct. 2004: 2 hours. NIIFK. SPb. Part 1. Pp. 106-108.

Nikolaev, 2012 – *Nikolaev, Yu.M.* (2012). About the change of paradigms of theoretical knowledge in the sphere of physical culture. *Theory and practice of physical cultures.* 10: 59-64.

Polyakova, 2012 – *Polyakova, T.D.* (2012). Formation of health preservation competence among students. Minsk: BGUFK. 105 p.

Stolyarov, 2012 – *Stolyarov, V.I.* (2012). About two concepts and systems of physical education in the process of its modernization. *Izvestiya PGPU im. V.G. Belinsky. Social Sciences.* 28: 1056-1062.

Venskovich, 2015 – *Venskovich, D.A.* (2015). Physical condition of female students of the second and third trimesters of pregnancy studying in a higher education institution. *Vesnik Vitsebskagadzyarzh University.* 1: 72-80.

Venskovich, 2015 – *Venskovich, D.A.* (2015). Theoretical and methodological prerequisites for the development of an educational cluster on physical culture of pregnant female students studying in a higher education institution. *World of sport.* 3: 31-37.