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Common genetic hair shaft abnormalities may be visualized by light and electron microscope

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Abstract: Abnormalities in keratin gene clusters either acidic cluster or basic cluster leads to hair shaft abnormalities. Hair shaft abnormalities can be divided into those with increased hair fragility or not associated with hair fragility

Objective: Light and electron microscopic studies of hair shaft abnormalities performed to better define, the microscopic changes seen in Hair shaft. Methods: Biopsy specimens were obtained from 13 patients, 11 children and 2 adults. The hair follicles were studied by light and electron microscopy.

Results: The results show that characteristic light microscopy features of Netherton syndrome, monilethrix, woolly hair syndrome, pilitorti, piliannulati and trichothiodystrophy and others may be visualized by light and electron microscopy.

Key words: Key words: hair shaft, Light, Electron Microscope.

Introduction

Hair shaft abnormalities encompass a group of congenital or acquired alterations which involve the hair shaft. Single gene disorders are characterized by hair abnormalities. Hair changes may be a significant fin- ding or even the initial presentation of a syndrome giving the clue to the diagnosis, in diseases such as trichothiodystrophy or Netherton syndrome [1-3]. They usually lack macroscopic features, which would enable easy diagnosis in medical practice. Thus, the usual diagnostic method is light microscopy and every time about 40 - 50 hairs are plucked to decrease the risk of missing a hair with the characteristic abnormality under light microscope [4]. The aim of this study was to verify whether hair shaft abnormalities may be visualized by light and electron microscope of common genetic hair shaft abnormalities.

Methods: A total of 13 of different hair shaft abnormalities these are (Netherton Syndrome and Monilethrix, Woolly hair

syndrome (WHS), Trichothiodystrophy, Acquired progressive kinking of the hair) In all patients, light microscopy evaluation When applicable, polarized light microscopy, scanning electron microscopy were perform considerably higher in the temporal and occipital area (90%), as compared to the vertex and parietal area of the scalp (40%).

Results: The results show that characteristic light microscopy features of Netherton syndrome, monilethrix, woolly hair syndrome, pili torti, pili annulati and trichothiodystrophy and others may be visualized by light and electron microscope. These genetic hair shaft abnormalities are

Atopy is commonly seen in affected individuals.

The breakage points consist of intussusceptions of the distal shaft ("ball") into the proximal shaft ("socket") due to defective cornification of the cortex. In adults, the scalp hair tends to improve but bamboo defects in the eyebrow and body hair may persist.

Monilethrix

Monilethrix is a term of Greek and Latin derivation meaning "necklace [6] hair". This disorder is inherited in an autosomal dominant fashion.

Normal appearing hair at birth, Later on, replaced by short fragile brittle hair.

Perifollicular erythema & follicular hyperkeratosis.

Hair has uniform elliptical nodes of normal thickness and intermittent abnormal constrictions. Monilethrix. Hypotrichosis due to breakage of fragile hairs. Note the small perifollicular papules with scale.

Mutation have been found in the genes that encode K83 and in patients with autosomal recessive form Desmoglein.

Usually, the scalp is the only region involved, but in more extensive cases there may be eyebrow, eyelash and nail involvement.

Netherton syndrome

Trichorrhexis invaginata and golf tee-like end were visualized by electron microscope. also known as bamboo hair [5].

Commonly seen in association with ichthyosiss linearis circumflexa in patients with Netherton syndrome. from pathogenic mutations in the SPINK5 gene.

Woolly hair syndrome (WHS)

Light microscopy revealed ovoid cross sections, 180-degree longitudinal twisting, trichorrhexis nodosa and pili annulate [7,8]. By scanning microscopy examination, the hairs were flat, appearing as oval or irregular on transverse sections with longitudinal and transverse grooves. In the distal end of the cuticle, cells were either damaged or absent, and the cortex and medulla were vacuolated.

Pili torti

Pili tortiis characterized by a flattened shaft and twisting of the hair fiber on its own axis [9].

Classic pili torti is part of a clinical syndrome. with ectodermal abnormalities (keratosis pilaris, nail dystrophies, dental abnormalities.

Bjrnstad syndrome associated with sensorineural hearing loss. Acquired pili torti-like hair shaft twisting has been reported in association with anorexia nervosa and oral retinoid therapy.

Menkes disease is an X-linked recessive disorder of copper metabolism.

Trichothiodystrophy

an autosomal recessive disorder characterized by sulfur-deficient hair [10].

marker for a neuroectodermal symptom complex.

alternating light and dark bands by polarizing microscopy.

PIBIDS refers to a phenotype consisting of: P (photosensitivity), I (ichthyosis), B (brittle hair), I (intellectual impairment with low IQ), D (decreased fertility) and S (short stature).

Acquired progressive kinking of the hair

Acquired curling of the scalp hair

young men develop curly, frizzy and lusterless hair in the frontotemporal region or vertex of the scalp [11].

Localized and diffuse forms. subsequent progression to androgenetic alopecia.

Loose anagen hair syndrome

The classic presentation is a young girl with fairly short blond hair that seldom needs cutting [12].

Anagen hair can be easily and painlessly pulled from the scalp microscopic examination reveals a ruffled proximal cuticle, absence of the root sheath, and a bent matrix result from faulty cornification of the inner root sheath. This would then interfere with normal interdigitation of the inner root sheath cuticle with the hair cuticle, leading to poor anchoring.

Pili bifurcati

This hair fiber anomaly is characterized by bifurcation of the hair fiber at multiple irregular intervals along the shaft [13].

forming separate rami, which then again fuse.

Each ramus has its own cuticle.

Pili multigemini

The term pili multigemini is associated with multiple hair shafts arising from one papilla [14].

Each hair fiber has its own inner root sheath. But all the fibers are surrounded by a common outer root sheath.

Multigeminate hairs are usually found in the beard region.

Spun-glass hair (uncombable hair)

This entity is also known as pili trianguli et canaliculi [15].

Hair is characteristically stiff and difficult to comb.

Abnormal keratinization of the internal root sheath is postulated to cause the irregularly shaped hair shafts. Which have a triangular shape on cross-section and a longitudinal groove that is best seen by scanning electron microscopy.

Discussion

The results of this study show that characteristic light microscopy features of most genetic hair shaft abnormalities may be visualized by light microscope and electronic microscope.

The Netherton syndrome is characterized by three major clinical features: ichthyosiform dermatosis (non-bullous ichthyosiform

erythroderma or as ichthyosis linearis circumflexa), atopy and a characteristic hair abnormality. Clinically hair appears sparse, dull, brittle and short. The hair shaft abnormality, called bamboo hair or trichorhexisinvaginata is microscopically characterized by an invagination of the distal portion of the hair shaft into its proximal portion forming a "ball in cup" appearance and is considered pathognomonic for Netherton syndrome. Occasionally ragged, cupped proximal hair end may be seen, where the fragile node has fractured. This abnormality is often referred to as "golf-tee hairs" [16,17]. The diagnosis of Netherton syndrome can be difficult. Often, there is no family history and concomitant atopy may lead to misdiagnosis of atopic dermatitis or severe

eczema. Differential diagnosis has to include Omenn's syndrome, generalized seborrhoeic dermatitis, erythrodermic psoriasis, staphylococcal scaled skin syndrome, non- bullous ichtiosiform erythroderma and atopic dermatitis [18]. The basis for diagnosis is microscopically confirmed trichorrhexis invaginata. Although a single hair with characteristic invagination is sufficient to establish the diagnosis of Netherton syndrome [19].

Monilethrix is an autosomal dominant hair disorder characterized by periodic thinning of hair shafts and a tendency to fracture at constricted points. This abnormality results clinically in hair fragility and patchy dystrophic alopecia [20]. The hairs are seldom longer than 5 to 8 centimeters. The effect of disease on hair is variable and may range even within families from close to normal or mild occipital hair loss to near total alopecia. Other hairy areas, such as the eyebrows, eyelashes, axillary hair, pubic hair and body hair may also be involved. Follicular abnormalities seen in monilethrix range from subtle perifollicular erythema and hyperkeratosis to horny follicular papule formation [21]. Mutations in hair specific keratins, especially hHb1 and hHb6, which are primarily expressed in cortical trichocytes, cause predominantly structure abnormalities of hair cortex. These are in particular multiple constrictions of hair shaft, which alternate with elliptical nodosities[22]. Despite characteristic microscopic findings, the disease is not simple to diagnose in dermatological practice, especially in mild cases of the disease. Recently, a case of a patient with monilethtix has been described, in which the diagnosis was first established at the age of 44.

Electroscopic imaging of the scalp and hair in monilethrix demonstrated an unusual picture of hair shafts with beaded appearance, bended regularly at multiple lo- cations with tendency to curve in different directions, giving it an appearance of a regularly bended ribbon.

The existence of pseudo monilethrix is an issue of controversy. According to some authors pseudo monilethrix is a hereditary hair weakness, in which hair shaft exhibit irregular artifactual thickenings or flattening [23]. Other authors suggest that true pseudo monilethrix does not exist and that sporadic occurrence of irregular hair shaft thickenings is an artifact produced by either procedure of pre- paring hairs for microscopic examination [24] or by excessive use of cosmetic hair care products.

Pili annulati is a rare hair shaft disorder characterized by discrete banding of hairs. The etiopathogenesis of this disorder remains unknown but it is likely to be a single gene defect [25]. It is often an incidental finding with alternating light and dark bands causing a slightly spangled appearance of the hair. The phenotype is variable, with not every hair affected, and with variability along a single hair shaft [26]. There is no association with hair fragility, however Gunter et al observed that with onset of hair thinning due to androgenic alopecia, progressive reduction of hair shaft diameter may cause increased fragility in pili annulate [27]. Light microscopy of pili annulati shows a random pattern of intermittent abnormal cavities. Light bands observed by clinical examination appear as dark bands when imaged by light microscopy. The spangled appearance is due to cortical spacer containing air in the light bands and fluid in the dark bands.

Pili torti is a rare hair shaft dysplasia due to a structural defect in which the hair shafts are flattened or ridged and twisted in their own axis, resulting in the clinical appearance of "corkscrew hairs" and in spontaneous breakage. Pili torti may be associated with many syndromes (Menkes, Bazex or Crandall syndrome) or may occur as an inherited, isolated phenomenon with the onset at birth or in the early months of life [28]. Acquired pili torti have been re- ported after treatment with oral retinoids.

In woolly hair syndrome the term "woolly hair" refers to an abnormal variant of fine, tightly curled hair that often exhibits decreased pigmentation. In 1974, Hutchinson et al. [29] classified woolly hair into 3 variants: woolly hair nevus, autosomal dominant hereditary woolly hair and autosomal recessive familial woolly hair. Since then, woolly hair has also been observed in association with several genetic conditions, especially the Noonan syndrome, which is characterized by short stature, typical facial dysmorphology and heart defects [30] and in the phenotypically overlapping cardiofaciocutaneous syndrome, which is characterized by congenital heart defect, developmental delay, peculiar facial appearance with bitemporal construction, prominent forehead, down slanting palpebral fissures, abnormalities of the skin and curly sparse hair [31]. Distinguishing woolly hair from curly hair may require evaluation of hair shafts by either light or electron microscopy [32]. Light microscopy revealed ovoid cross sections, 180-degree longitudinal twisting, trichorrhexis nodosa and pili annulati. Scanning electron microscopy revealed hairs which were flat, appearing as oval or irregular on transverse sections with longitudinal and transverse grooves. In the distal end of the cuticle cells were either damaged or absent and the cortex and medulla were vacuolated.

From all evaluated hair shaft diseases, only in the case of trichotiodystrophy is trichoscopy insufficient for making the diagnosis.

Conclusion

In conclusion, our study shows that in all hair shaft abnormalities with the exception of trichotiodystrophy.

Trichothiodystrophy, or sulfur-deficient brittle hair, identifies a group of rare and complex neuroectodermal disorders with remarkable clinical heterogeneity [33].

Clinical symptoms of trichothiodystrophy vary widely in nature and severity, and the single common feature in all patients is fragile hair. Scalp hairs, eyebrows and eyelashes are brittle, unruly, of variable lengths. With polarizing microscopy, using crossed polarizers, hair shafts show a distinctive hair feature: striking alternating bright and dark bands, often referred to as "tiger tail" banding.

Light microscopy showed hair shafts with an irregular, undulating contour and clean transverse fractures through the hair shaft (trichoschisis). The basis of this undulation is not understood, although it may reflect a weak and unstable internal cortical structure, a consequence of the major reduction in disulfide crosslinking, reflected by the low total sulfur content. Cross-sectional examination of the cuticle in hair shows lack of the exocuticle and A layer [34].

The bright and dark bands seen with polarized light correspond to the undulating orientation of the cortical fibers in Trichotiodystrophy. Hair shafts

are notably flattened and may fold over like ribbon during the hair mounting process [33].

In general, it has to be pointed out that for investigating a possible hair shaft abnormality ex vivo, an appropriate sample of hairs must be collected. Hairs must be in sufficient amount to provide a reasonable chance of finding relevant positive clues. A sample of 40-50 hairs is usually adequate to allow detection of most significant abnormalities. There are exceptions, and Netherton's syndrome is one, where repeated samples of several hundred hairs may be needed to confirm the diagnosis.

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Effect Of Video Teaching On Home Care Management Of Mothers Preterm And Low Birth Weight Baby

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Abstract: Preterm and low birthweight babies are forced to extra utriene environment before the physical and social development of the neonate.They are fragile unstable and require life support in a and highly technological care.They are shifted to neonatal intensive care unit soon after birth for specialized care.In the neonatel intensive care unit babies are receiving high technological care by qualified health perssonal. Soon after the baby discharge from the NICU mothers are the primary care giver to rearing the child. So mother need some kind of empowerment on baby care during the stay of hospitalization its self by health personnalespecially for NICU babies.The present study is aim to assess effectiveness of video teaching on knowledge of mothers on home care management of preterm and low birth weight baby admitted in NICU. The study was conducted at PPK hospitalMarthandam. A sample of 110 mothers were selected using purposive sampling technique. Knowledge score was assessed by using structured questioner. Data were gathered by self administered method. Dataanalysis was done by using descriptive and inferential statistics.

Key word: Post natal mother ,knowledge ,neonatal intensive care unit, home care managment.

The birth of a baby is a wonderful yet very complex process. After birth Many physical and emotional changes occur for mother and baby. A baby must make many physical adjustments to life outside the mother's body .Parents are the most crucial and immediate environment in which the newborn survives and develops.

The prevalence of preterm and low birth weightbbaby is increasing worldwide. More than one in ten babies are born preterm annually. This is equal to 15 million preterm infants born globally and the second largest direct cause of deaths in children below five. The highest rates of preterm birth are in Sub-Saharan Africa

and South Asia (more than 60%) and the lowest rates are in Northern Africa, Western Asia, Latin America and the Caribbean. The preterm birth rates in the developing countries vary widely and follow a different pattern than in high income countries. The majority of the preterm 84.1% are born between 32 to 37 week and may have significant medical problems requiring prolonged hospitalization.

India has the daunting task of caring for more newborn infants than any other country in the world. At present 1.2 million of them die before completing four weeks of life .Almost 8 million LBW and preterm infants are born in India every year. Birth weight is the single most important marker of adverse prenatal, neonatal and infantile outcomes.

Newborn babies who need intensive medical attention are often admitted into a special area of the hospital called the Neonatal Intensive Care Unit (NICU). The NICU combines advanced technology and trained health care professionals to provide specialized care for the baby. Most babies admitted to the NICU are premature (born before 37 weeks of pregnancy), have low birth weight (less than 5.5 pounds), or have a medical condition that requires special care.

The management of preterm birth in NICU by health personal is very important to improve the health condition, prevent complication, morbidity and mortality. Very small babies a special care unit where essentially emphasis is given on intensive care, observation, management of feeding, infection free atmosphere and prompt skillful management of supervening complication.

Advancement in NICU technology has led to better survival of these neonates, therefore they can impose heavy emotional and financial burden on the families. Mothers pay not only for NICU hospitalization, but also the high price of utilizing medical care after discharge. Mother's whose neonate is kept separate from them, show high level of stress, fear and hopelessness. The problems are usually the result of inadequate knowledge of mothers about how to perform their parent role during and after hospitalization.

Maternal self-perceived incapacities and incompetence in parenting responsibilities is one of the greatest sources of psychological stress. Mother s knowledge on preterm and low birth weight baby especially after discharge from NICU is very essential to care the baby. So they need some kind of educational intervention.

The investigator observed the recurrent readmission of low birth weight babies due to infection and with other health problems especially among very preterm and very low birth weight baby. It mainly due lack of knowledge and confidence of mother to care the baby. It was mainly noticed among NICU admitted baby. The poor parental knowledge on home management has resulted in poor child rearing practice, frequent hospitalization and an increase in mortality and morbidity rate.In addition financial factors and working status of mother also influence the parent to get early discharge from NICU. Increasing the knowledge and awareness about the preterm and low birth weight baby care enable the the person to deal with un expected stress full situation during and after hospitalization.

Objective of This Study

1. To assess the knowledge on home caremanagement among mothers of preterm and low birth weight babies admitted in NICU.

2. To find the effectiveness of video teaching on home caremanagement among mothers of preterm and low birth weight babies admitted in NICU.

3. To find the associationbetween the knowledge scores of mothers of preterm and low birth weight babies and their demographic variables.

Hypothesis

There will significant difference in thebetween pretest andpost test knowledge scores of mothers after viedo teaching

Methodology

Research approach:-

Research approach of this present study is descriptive in nature.

Research design:-

Research design of this study was quasi experimental research design. One group pretest and post test design

Research setting

PPK hospitalMarthandamkanyakumari. district

Sampling and sampling technique

Samplewere selected using purposive sampling technique. Totally 110 sample were selected for the study

Inclusion criteria

Mother can read and understand tamil

Mothers of preterm and low birth weight baby admitted in NICU

Exclusion criteria

Mothers who are not willing to participate

Mothers who are seriously ill at the time of data collection

Research tool

Structured self administered questioner was used to collectthe data.It contains 20 question relavent to home care management of preterm and low birth weight baby

Data analysis

Table-1: Percentage distribution of selected demographic variables of mothers of preterm and low birth weight baby

Demographic profile	Component	sample n= 110 Freq	%	Results	Sig
Age Group (years)	<20	8	7.3	χ^2=9.579 df=4	P=0.059
	20-24	34	30.9		
	25-29	38	34.5		
	30-34	25	22.7		
	35+	5	4.5		
Educational status	High Sl	4	3.5	χ^2=2.876 df=3	P=0.411
	Hr. Sec	26	23.6		
	Graduate	71	64.5		
	PG	9	9.0		
Occupational status	Employed	31	28.2	χ^2=0.916 df=2	P=0.633
	Self	12	10.9		
	Unemployed	67	60.9		
Family income (000)	5-10	3	2.7	χ^2=0.998 df=3	P=0.802
	10-15	29	26.4		
	15-20	53	48.2		
	20+	25	22.7		
Family Type	Nuclear	41	37.3	χ^2=4.401 df=2	P=0.111
	Joint	62	56.4		
	Extended	7	6.4		
Care takers	Mother	69	62.7	χ^2=3.084 df=3	P=0.379
	Husband	10	9.1		
	In-laws	28	25.5		
	Others	3	2.7		
Birth order	1st	46	41.8	χ^2=3.592 df=2	P=0.166
	2nd	59	53.6		
	3rd	5	4.5		
Previous NICU	Yes	6	5.5	χ^2=0.096 df=1	P=0.757
	No	104	94.5		
Gestational age (weeks)	Preterm	31	28.2	χ^2=4.437 df=1	P=0.035
	Low birth baby	79	71.8		
Health care	Medical ill	94	85.0	χ^2=6.088 df=1	P=0.014
	Pre term care	16	15.0		

Table-2 Assessment of knowledge of mothers on preterm and low birth weight baby in pretest:

Level of knowledge	Pre test	
	Freq	%
poor	0	0.0
Moderate	110	100.0
Good	0	0.0

In the above table-2, shows the knowledge of mothers on preterm and low birth weight baby in pretest. At pre

test all 100% of mothers had moderate stress.

Table-3: Assessment of knowledge of mothers on preterm and low birth weight baby in post test

Level of knowledge	Post-2 test	
	Freq	%
Poor	0	0.0
Moderate	2	1.8
Good	108	98.2

Table 3 shows the knowledge of mothers on preterm and low birth weight baby in post test in post-2 test indicated that 1.8% mothers had moderate knowledge and the remaining 98.2% had good knowledge .

Table-4:Effects of viedo teaching on knowledge of mothers on preterm and low birth weight baby

Levels (tests)		Level-I		Level-II		improvement		"t"	df	Sig
I	II	Mean	SD	Mean	SD	Mean	SD			
Pre	Post-2	16.9	1.6	23.8	1.8	6.9	1.9	37.965	109	P<0.001

Table-5: shown the effect of video teaching on knowledge of mothers pretrm and low birth weight in relation to home care management The mean pre test was 16.9 and the post test was 23.8 with mean improvement from pre through post test was 6.9±1.9. Theimprovements was statistically very highly significant (P<0.001).

RESULTS AND DISCUSSION

The study findings revealed that in pretest all of the women had (100 %) moderately adequate knowledge and none of them had adequate knowledge regarding home care of preterm and low birth weightbaby. With regards to posttest 2(1.8 %)of them had moderately adequate knowledge 108 (98.2 %) of them had adequate knowledge.The analysis also revealed that resut are statistically very highly significant at P<0.001level.The findings showed that there was a significant improvement in the level of knowledge on home care management of preterm and low birth weight baby after administration of video teaching .

The demographic variables like education occupation and type of family in mothers of preterm and low birth weight were associated with the level of p value p<0.05. All the other demographic variables are not associated mothers knowl;edge. The finding of the study was supported by the below study

Venu A.S, and Shilpa G.K, (2016) were conducted a study to assess the Effectiveness of structured teaching programme on knowledge and practice of common newborn care among primi mothers. The results revealed that mean knowledge scores in pre-test were 6.5 and SD was 1.58 and in post-test mean was 18.5 and SD was 3.54. So, it is evident that mean post-test knowledge score of primi mothers were significantly greater than their mean pre-test knowledge score after video teaching.

Nursing implications:

Women are the important person in the world, since they are carrying the fetus during the antenatal period anggiving human assert to the world.Each and every women face lot of physical and psychological problem during pre and post natal period. Post natal mother were worried and anxious about the new born health condition if the baby born preterm and low birth. Parents also anxious about prognosis and how to parenting them after NICU discharge. It is very essential to teach the parent about home care management inorder to prevent infection and readmission to NICU.

- NICU nurses can give routine health education to all mothers of preterm and low birth weight baby.

- Impart knowledge about preterm care, NICU equipment NICU care and nature of treatment by NICU personal will help to reduce stress , enhance coping and confident.

- Pamphlet can be given to all mothers of preterm regarding importance of home care of baby after NICU admission.

- Family centered care in the NICU is encouraged when ever possible.

- NICU staffs are to be given regular in service educationprogramme to gain adequate Knowledge and development positive attitude. It helps in planning individualized and family centred careabout home care of preterm and low birth weight baby.

CONCLUSION:

The present study revealed the importence of adequate preparation of mother to care the baby after discharge. Health personal working in NICU must aseessthe level of knowledge and provide adequate knowledge and psychological support will help them to overcome their problem and lead quality life.

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Resistance To Antibacterial Drugs Of Community-Acquired Urostrain Escherichia

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Abstract: Of the 426 outpatients examined with UTI, microbial growth in the urine in diagnostic titers (103, often 104 -105 CFU /ml) was obtained in 165 patients. Of the isolated isolates, 143 (87.7%) belonged to the Enterobacteriaceae family, 112 (78.3%) were to typical E.coli. Determination of the sensitivity of E. coli to 26 antibiotics was performed by conventional and screening phenotypic methods. Sensitivity to five fluoroquinolones ranged from 57.6% to 45.6%. Amikacin, gentamicin, chloramphenicol and tigecyclinwere more effective - 72,3%, 60% 85,5% and 73%, respectively. 40,3% of the strains were resistant to trimethoprim-sulfamethoxazole. Even higher resistance of escherichia was found in relation to ceftibuten (93.2%) and cefixime (81.0%), by contrast, nitrofurantoin and fosfomycin were sensitive in 100% and 95.9% of cases. In E.coli, resistant to basic cephalosporins of the 3rd generation, the production of ESBL was confirmed by the method of combined disks in 25 strains. InE.coli, resistant to imipenem and meropenem, the production of carbapenemases was confirmed by the biochemical method CARBA BLU in 50.0% of cases (10 strains from the 20s).

Keywords: Escherichia, urostrain, resistance, antibiotics

Introduction

Urinary tract infections (UTIs) are spreading worldwide, both in nosocomial and extra-hospital environments [7,5,8,11]. Numerous publications note that E. coli, which are the dominant causative agents of UTI, are characterized to develop resistance to antibacterial drugs [2,14,16,17,18], with the greatest problems associated with resistance to beta-lactams and fluoroquinolones[9,20]. For the treatment of community-acquired

UTIs, various standards of empirical therapy for the choice of oral antibiotics of the 1st or 2nd line are proposed [2,5,10,13,19], but adequate antibacterial therapy requires data on the sensitivity of local strains of pathogens to the recommended antibiotics. Moreover, knowledge of circulation among non-hospitalized patients with UTI of Escherichia producing enzymes that are responsible for the resistance to beta-lactam antibiotics - beta-lactamase extended spectrum (ESBL) and various carbapenemases (KPC, MBL, etc.) is important.

Purpose of the study.Determination of the resistance to modern antibiotics of extra-nosocomial-acquired urostrains of E.coli using traditional and screening phenotypic methods.

Materials and methods. 426 patients who applied to the private "Vitras" diagnostics center (VITROSDIAG-NOSTICS LLC) over the period from October 2017 to March 2018 were examined with the diagnosis of acute uncomplicated urinary tract infection (UTI). Among them, women were 358 (84%), men 68 (16%). The urine of the patient was examined by Gould's sectoral method, microorganisms, growing in urine dilution no less than 103CFU/ml, were referred to the causative agent of the infection. From each patient, only one strain was included in the study, repeated isolates were ignored. The identification of the isolated cultures was carried out by conventional methods [1]. The sensitivity of isolated isolates to 26 antibiotics was determined by the disc-diffusion method (DDM) using the M?ller-Hinton medium, the McFarland standard and commercial antibiotic discs (HiMedia), and the study was conducted in accordance with the EUCAST standards [4]. When assessing the borderline valuesof the antibiotic thediameter of zone of inhibition (DZI), new recommendations from the European International Guidelines were used [13]. The internal quality assurance of antibiotic susceptibility testing was carried out with a reference toE. coli strain ATCC 25922. In Escherichia, which were screened with 3 basic cephalosporins (CP), suspicious for the production of ESBL, a confirmatory test was performed with a combination disk with ceftazidime with ceftazidime/clavulanic acid and ceftriaxone with ceftriaxone/clavulanic acid. According to the method, the expansion of the diameter of thediameter of zone of inhibition (DZI) of the culture under study around a combined disk in comparison with a disk without inhibitor by 5 mm or more (synergism) indicates the production of ESBL (4).In Escherichia, suspicious of the production of carbapenemases (in screening in DDM with 3 carbapenems), the confirmatory test was carried out using the Nordmann P. method [12] in the modification of PiresJ. - the CARBABLU method [15]

Results.Of the 426 patients examined with UTI, microbial growth in the urine was found in 220, but in 55 patients (12.9%) either single colonies were detected, or up to 102CFU/ml. In diagnostic titers, microorganisms showed an increase in 165 patients (38.7%), and in most of these urine samples microorganisms grew in titers of 104-105 CFU/ ml. and higher. The isolated isolates 143 (87.7%) belonged to the family of Enterobacteriaceae, 112 (78.3%) of them belonged to E. coli. According to morphological, cultural and biochemical properties, all strains of Escherichia

corresponded to their species characteristics. It should be noted at once that according to EUCAST (2018), the zones of growth retardation of enterobacteria for a number of antibiotics have been revised and for the category "sensitive" zones expanded by 1 mm or 2 mm - for ceftriaxone, aztreonama, ofloxacin, levofloxacin, moxifloxacin; 3 mm for cefepime and 4 mm for ciprofloxacin; for 2 other antibiotics of the growth retardation zone, narrower ones are suggested for 2 mm - for ticarcillin-clavulanate and sulfamethoprim-sulfomethoxazole.

Resistance to betalactams will be considered below, in table 1 data on the antibiotic susceptibility of E. coli to fluoroquinolones, aminoglycosides and other antibacterial drugs are presented.

Table 1.Antibiotic sensitivity of community-acquired uropathogenicE.coli to antibiotics of different groups

Antibiotics	Numberofstrain sstudied	S	RS	R
Fluoroquinolones:				
Ciprofloxacin	90	45,6%(41)	20,0%(18)	34,4(31)
Norfloxacin	78	51,3%(40)	2,6/% (2)	46,1% (36)
Ofloxacin	90	44,5%(40)	10,0%(9)	45,5%(41)
Levofloxacin	90	46,6%(42)	16,7%(15)	36,7%(33)
Moxifloxacin	85	57,6%(49)	1,2%(1)	41,2%(35)
Aminoglycosides:				
Gentamicin	89	67,4%(60)	14,6%(13)	17,9%(16)
Amikacin	83	72,3%(60)	15,7%(13)	12%(10)
Tetracyclines:				
Tetracycline	88	52,3%(46)	1.1%(1)	46,6%(41)
Doxycycline	90	48,9%(44)	5,5%(5)	45,6%(41)
Othergroupsofantibiotics				
Trimethoprimissulfamethoxazole.	67	59,7%(40)	1,5%(1)	38,8%(26)
Chloramphenicol	89	69,7%(62)	-	30,3%(27)
Phosphomycin	49	95,9%(47)	-	4,1%(1)
Nitrofurantoin	47	100%(47)	-	-

Legend: S-sensitive, RS - mild-resistant, R-resistant. In ()- are absolute digits

As can be seen, all five tested drugs of the fluoroquinolone series showed approximately the same results: the sensitivity of the urostrains of E. coli ranged from 57.6% to 45.6%. It should be noted only a high level of moderately resistant strains with respect to ciprofloxacin, levofloxacin and ofloxacin is likely that these results are associated with the extension of growth retardation zones when evaluated in DDM [3]. The sensitivity of community-acquired E.coli to aminoglycosides: amikacin was more active (72.3%) than gentamicin (60.0%); in 17.6% and 15.7% of the Escherichia showed themselves as moderately resistant to these antibiotics. Sufficiently high sensitivity (70%) of escherichia has been shown with respect to chloramphenicol, although it refers to "old" and widely used drugs. Despite the fact that tetracycline and doxycycline are excluded from the list of EUCAST [3], we give the results of their testing and, as can be seen from Table. 1, their activity was 52.3% and 67.4%, respectively. A special place is occupied by tigecycline - one of the relatively new drugs of a wide spectrum of action - 85.5% of the strains studied were sensitive to it. To trimethoprim-sulfamethoxazole, 40,3%of the strains were resistant, according to the recommendations of the European Urological Association (EAU), it can not be used for local resistance in more than 20% of the Escherichia. An even higher resistance of Escherichia was found for ceftibutene (93.2% of the 44 studied) and cefixime (81.0% of the 47 studied), while they are recommended as first-choice drugs for the empirical treatment of community-acquired UTIs [2,13].

Highly active were antibiotics, which are recommended in almost all Guides and publications as first-line drugs for the treatment of UTI: nitrofurantoin 100%, fosfomycin 95.9% of susceptible strains.

Next, we present the results of a study of the effects of betalactams on community-acquired E. coli. Ampicillin was resistant to 65% of strains, of the 3 inhibitor-protected penicillins, ampicillin-sulbactam (65% of sensitive strains) was most active, 72.0% of the strains were resistant to ticarcillin-clavulanate and amoxicillin-clavulanate, although the latter was suggested for asymptomatic bacteriuria in pregnant women [19].

The following figure 1 presents data on the antibiotic resistance of the uropathogenicE.coli to aztreonam, as well as to the 3rd generation cephalosporin and to the 3 carbapenems, the basic antibiotics used for routine screeningof the microorganisms products ESBL and carbopenemase (EUCAST).

Fig-1

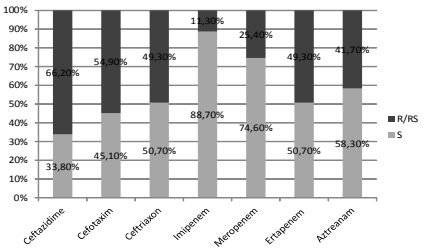

Fig-1 Resistance of community-acquired uropathogenicE.coli to beta-lactam antibiotics

From the figure it is clear that community-acquired Escherichia showed resistance - from 49.3% to ceftriaxone to 66.2% to ceftazidime. In the group of carbopenem antibiotics, imipenemwas the

most effective, to which resistance was found only in 11.3% of the strains. There were more resistant strains to meropenem (25.3%), but among them almost a third (27.7%) was moderately resistant. About half of the studied strains (49.3%) were resistant and moderately resistant to ertapenem, and similar results were obtained for aztreonam (monocyclic beta-lactams) - 41.8% of resistant strains. The low efficacy of in vitro of two beta-lactam antibiotics with respect to hospital Escherichia was described by us earlier [9], and in further studies it is necessary to find out whether these "exceptional" (according to EUCAST terminology) phenotypes are a regional feature of our region.

In total, out of 71 E. coli strains isolated from the urine of non-hospitalized patients with UTI, according to preliminary screening in DDM (resistance to ceftazidime, cefotaxime, ceftriaxone), 59 strains (83.1%) were suspicious of production for ESBL. Of these, 15 strains were resistant to only one of the tested antibiotics - most often to ceftazidime (10 strains); 12 - in parallel to two cephalosporins; The 32-strain was resistant to all 3rd cephalosporins at the same time.

In these 32 strains of E. coli, a confirmatory phenotypic test was performed with commercial combination discs (see Methods). A clear positive result was obtained in 25 of the 32 strains studied, in 5 strains the synergy zone was less than 5 mm by 1-2 mm, and in 2 isolates was absent.Below is a photo of the test results with combined disks in 3 cultures.

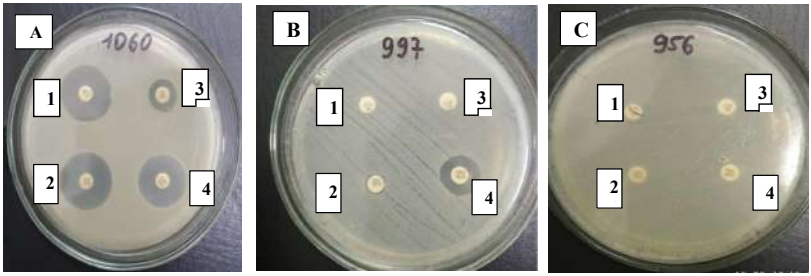

Photo - 1 Combined disc method for confirming ESBL production 1. Cefotaxime 2.Cefotaxime / clavulonic acid 3.Ceftazidime 4.Ceftazidime / clavulonic acid. A and B ESBL - positive; C-ESBL- negative

The preliminary selection of strains in DDM for the production of carbapenemases is carried out according to the same procedure as for ESBL - the study is carried out with 3 carbapenemase antibiotics - imipenem, meropenem, ertapenem. In our our collection of Escherichia suspicious for carbapenemase products, there were 42 (59.1%) strains for the production of carbapenemases, but of these, 20 strains were resistant only to ertapenem, while among them 14 were moderately resistant.Considering this, we attributed 22 (31%) E. coli strains to probable producers of carbapenemases, of which 3 isolates with simultaneous resistance to 3 carbapenems, and to 2 carbapenems (imipenem and

meropenem) 19 isolates. To confirm carbapenemase productsof specified 20 strains of community-acquired Escherichia were used biochemical method CARBA BLU method [3,15].The principle of the method is simple - if the microorganism produces carbapenemase (cattle or MBL - VIM, IMI, NDM), this enzyme hydrolyzes the antibiotic in the medium to form acidic products and change the color of the indicator from blue to yellow. In parallel, the experimental samples were set to control with the reference E. coli strain ATCC 25922, which does not produce carbapenemases. Clearly positive results were obtained in 10 studied E.coli strains.

Conclusions

1 The high resistance of local community-acquired E. coli urostrains to oral beta-lactams - cefexim (81,0%) and ceftibuten (93.2%) -is established, while nitrofurantoin and phosphomycin remain highly effective preparations - 100% and 95.9% sensitive strains.

2. The outpatient E. coli urostrains in ordinary DDM were suspicious of ESBL products in 83.1% of the 71 studied; in case of selective confirmatory testing with combined disks of 32 strains (all simultaneously resistant to the 3rd cephalosporins), the probable producers of ESBL are assigned to.

2. Community-acquired urostrains in conventional DDM were suspicious of carbapenemase products at 59.1%; with selective confirmatory testing of 20 isolates (at the same time resistant to imipenem and meropenem) by the CARBA BLU method, 50% were assigned to producers of carbapenemases.

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Studying Emotional States And Quality Of Life In Patients With Chronic Heart Failure

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Abstract: This article discusses the general aspects of studying the development and progression of psychological states in chronic heart failure. During recent years, more and more evidence is accumulating that depression is an independent risk factor for CHD and should be considered on a par with dyslipidemia, hypertension, and smoking. Cardiovascular diseases were one of the first sections of clinical medicine where large-scale quality of life studies began. On the one hand, this is due to the high prevalence of this pathology, on the other hand, because the quality of life in patients with diseases of the heart and blood vessels is an important criterion for the severity of the condition and the effectiveness of the therapy.

Key words: Coronary heart disease, chronic heart failure, dyslipidemia, alexithymia, deconditioning, quality of life, depression, arterial hypertension.

Among the diseases most dangerous for the life and health of the population of our planet in the coming years, the first places belong to coronary heart disease (CHD) and depressions. The combination of these diseases significantly worsens the clinical and social prognosis of each of them. The proportion of patients suffering from anxiety-depressive disorders among IHD patients varies from 12 to 47%. At the same time, the initial level of depression and personal anxiety in this category of patients is an even more significant factor affecting the quality of life than the number of coronary arteries with more than 50% occlusion. Chronic heart failure is a disease with a complex of characteristic symptoms (shortness of

breath, fatigue, decreased physical activity), which are associated with insufficient blood supply to the organs by the blood at rest or during exercise, and are often accompanied by fluid retention in the body. The basis of chronic heart failure is a decrease in the ability of the heart to fill or empty, due to damage to the muscles of the heart, as well as an imbalance of systems that affect the cardiovascular system.

During recent years, more and more evidence is accumulating that depression is an independent risk factor for CHD and should be considered on a par with dyslipidemia, hypertension, and smoking. It was found that not only the formed depression, but also the presence of its individual symptoms, are the pathogenetic link of cardiovascular diseases, which is no less important than the secondary emotional response to the disease.

Statistics show a steady increase in the number of CHF cases in all countries, regardless of the political and economic situation. Facts about the prevalence of heart failure by the mid-90s: the prevalence of clinically severe CHF in a population of at least 1.8-2.0%.

The emotional state of the patient is especially important in the post-infarction period. Many publications in our country and abroad are devoted to the influence of the socio-psychological status and the integral indicator "quality of life" on the course of CHD after an acute myocardial infarction. In particular, a direct link between the quality of life and the development of recurrent myocardial infarction and / or its recurrent course is shown. It has been established that depression is a reliable prognostic sign of death within 6-18 months after the development of myocardial infarction, increasing the mortality rate of such patients by 4 times. The primary cause is the deterioration of the ability of the heart to fill or empty, due to myocardial damage, as well as an imbalance of the vasoconstrictor and va sodilating neuro humoral systems" [1, p. 65].

Disadaptive syndromes, depressive, anxious and depressive states are associated with worse treatment adherence. They are also associated with an unhealthy lifestyle - smoking, eating disorders, physical inactivity, excessive use of alcohol and other psychoactive substances [2, 3].

From this point of view, such psychological characteristics of the patient as alexithymia are of great interest. According to the modern interpretation, alexithymia suggests: difficulties in determining one's own feelings, as well as differences between feelings and body sensations [4].

Anxiety and depressive disorders are a risk factor for heart disease, but an inverse relationship has also been proven.

For example, anxiety disorders play an important role in the occurrence of cardiac arrhythmias. V.V. Murashko and co-workers at an experimental-psychological study revealed significant differences in the personal profile of MMPJ in patients with coronary artery disease with and without arrhythmias, indicating a lack of effectiveness in alleviating anxiety and deep personality disharmony among the first. More than a quarter of patients with supraventricular and ventricular arrhythmias were diagnosed with anxiety-phobic and depressive syndromes [5]. In addition to anxiety-depressive disorders, the type of personality D (distressive), including negative excitability (a tendency to

experience negative emotions) and social suppression (suppression of emotions and behavioral reactions during social interactions) have recently been attributed to psychological risk factors. In recent studies, it has been shown that the presence of a type of personality D adversely affects the course and prognosis of patients after myocardial infarction [6].

Diseases of the cardiovascular system for many years are the main cause of mortality in many economically developed countries. Mortality from diseases of the circulatory system in the Russian Federation annually accounts for 55-57% of the total mortality [7], of which about half is caused by coronary heart disease and arterial hypertension.

The interest of modern medicine in studying the quality of life can be explained by the following reasons [8]:

- One of the fundamental principles of modern medicine is respect for the personality and rights of the patient, including the preservation and maintenance of the highest possible level of physical, mental and social well-being for each patient.

- The overall morbidity structure has changed in recent decades: among the diseases of the therapeutic profile (and especially in the field of cardiovascular diseases), chronic processes prevail, respectively, the number of chronic (for the whole life of suffering) patients prevails. Given the impossibility of achieving effective etiotropic treatment for such patients, therapy should be aimed at improving their quality of life.

The World Health Organization describes the quality of life associated with health as "individual perception of one's position in life in context with the cultural environment and value system in which an individual lives and in relation to his goals, expectations, standards and views" [9].

Currently, there are five main components of the quality of life that are relevant to health: 1) physical condition (physical limitations, physical abilities, physical well-being); 2) mental state (levels of anxiety and depression, psychological well-being, control of emotions and behavior, cognitive functions); 3) social functioning (interpersonal contacts, social connections); 4) role functioning (role functioning at work, at home); 5) the general subjective perception of the state of one's health (assessment of the present state and its prospects).

Uniform generally applicable criteria and standards for the study of quality of life does not exist. The assessment of the quality of life is influenced by age, gender, nationality, the socio-economic situation of a person, the nature of his work activity, religious beliefs, cultural level, regional characteristics, and many other factors. This is a purely subjective indicator of objectivity, and therefore the QOL assessment of respondents is possible only in a comparative aspect (the patient is healthy, the patient of one disease is sick of another disease) with the maximum leveling of all external factors [10].

According to the World Health Organization, the category of health includes the categories of physical, mental, spiritual and social health. Therefore, to assess the quality of life, one should use such a tool that would cover various aspects of the quality of life, be sensitive to changes in health status, the results should be comparable with other dimensions of health status, clinical status. An important requirement

is the possibility of its use in people of different sex, age, regardless of occupation, nature of the disease. At the same time, it should be a simple, concise, easy-to-understand document, allowing to obtain a quantitative assessment of the parameters being studied. The result of the active work of international research groups over the past decades has become a consensus on standardized interviewing [11, 12].

The most rational is the use of questionnaires (questionnaires) and tests. The use of standardized questionnaires (indices and profiles) is necessary for obtaining comparable results. The important components of standardization include the psychometric properties of the instrument: reliability, validity, and sensitivity: reliability is the ability of the questionnaire to provide constant and accurate measurements; validity (validity) - the ability of the questionnaire to reliably measure the main characteristic that it contains; sensitivity (sensitivity to change) - the ability of the questionnaire to give significant changes in the QOL score in accordance with changes in the respondent's state (for example, during treatment). A patient, a doctor, or specially trained personnel can fill out the questionnaire [13].

Questionnaires designed to assess QOL of patients with various diseases in children and adults fall into the category of general questionnaires, they are applicable for population-based studies, but, as a rule, are not very sensitive. In addition to general questionnaires, special disease-specific questionnaires were developed for the study of QOL in the fields of medicine, nosology, and the specifics of certain conditions. Special questionnaires are highly sensitive, but their scope is limited to a narrow specific area [14].

Depending on the structure, they identify profile questionnaires (several digital values, which are profiles formed by scale values) and indices (a single digital value). For the construction of general techniques known by a specialist in the field of studying the quality of life, Ware J.E. it was proposed to allocate sections related directly to the characteristics of the patient. In total, four such blocks are formed (physical, emotional, social sphere and general subjective perception of health). And one block, according to the researcher, should reflect the parameters specific to a particular pathological process, including biomedical technologies, etc. [15]. Such an approach is laid down in standardized quality of life assessment methods such as Sickness Impact Profile (SIP), General Health Rating Index, Nottingham Health Profile (NHP), Nottingham Health Profile, NHP, Poppy Master Questionnaire The McMaster Health Index Questionnaire, the Quality of Life Index and other general questionnaires. The wide range of the listed KKZH questionnaires reflects the urgent needs of the practice in a differentiated approach to the assessment of the patient's condition in various diseases. Questionnaires that are sensitive to assessing the quality of life in some diseases may be insensitive to others [16].

In recent years, many clinical studies have successfully used SF-36 (born The Short Form-36), authored by John E. Ware. SF-36 consists of 36 questions grouped into eight scales: physical functioning, role-playing, body pain, general health, vitality, social functioning, emotional state, and mental

health. The indicators of each scale are compiled in such a way that the higher the value of the indicator (from 0 to 100), the better the score on the chosen scale. They form two parameters: the psychological and physical components of health [17].

Important information a physician-researcher working with certain groups of patients can get with the help of disease-specific questionnaires, which are used to assess the quality of life of patients suffering from certain diseases. With the help of special questionnaires, one category of quality of life (physical or mental condition), or QOL for a specific disease, or certain types of treatment are assessed. The most frequently used special questionnaires in cardiology are: The Seattle quality of life questionnaire for angina (Seattle Angina Questionnaire); Questionnaire for assessing the quality of life for angina (Angina Pectoris Quality of Life Questionnaire); Questionnaire for the assessment of specific activity (Specific Activity Questionnaire); Questionnaire for assessing the quality of life after myocardial infarction (Quality of Life after Myocardial Infarction); Questionnaire for assessing the health profile in cardiology (Cardiac Health Profile). Each questionnaire differs in the scope of research, the time required to complete the questionnaires, methods of filling in and quantify the indicators of quality of life. Most questionnaires have been translated into all major languages with appropriate adaptation to them [18].

The study of the quality of life in patients suffering from cardiovascular pathology is currently of great scientific and practical interest in assessing the effectiveness of diagnostic, therapeutic and preventive measures. Indicators of quality of life, as well as the characteristics of the picture of the disease, vary over time depending on the condition of the patient, which allows monitoring of the treatment being conducted, and, if necessary, its correction. Most of the techniques created to study the quality of life include the study of the physical and mental state, social constraints, role-playing and subjective perception of one's condition. The study of the influence of the disease on the patient's quality of life is based on the study of the patient's self-assessment of the limitations arising from a particular disease. Obtaining such data is possible with the help of a survey, filling in questionnaires, questionnaires, tests or scales [19].

In the Russian national recommendations of the Society of Specialists in Heart Failure and the All-Russian Scientific Society of Cardiologists for the diagnosis and treatment of CHF, this pathological condition is defined as "a disease with a complex of characteristic symptoms (shortness of breath, fatigue and decreased physical activity, edema, etc.) that are associated with inadequate perfusion organs and tissues at rest or under load and often with fluid retention in the body.

Cardiovascular diseases were one of the first sections of clinical medicine where large-scale quality of life studies began. On the one hand, this is due to the high prevalence of this pathology, on the other hand, the fact that the quality of life in patients with diseases of the heart and blood vessels is an important criterion for the severity of the condition and the effectiveness of the therapy [20,21].

Quality of life is an integral characteristic of the physical, social and psychological functioning of the patient.

In accordance with the above definition of health, WHO defines QOL as an individual's correlation of his position in society, in the context of his culture and value system with the goals of the individual, his plans, possibilities and degree of disorder. As can be seen, the fundamental properties of quality of life are the complexity and subjectivity in the assessment [22].

Considering that methodological guidelines for studying the quality of life are given by philosophical anthropology, and specific knowledge forms the medical sciences, it is advisable to define the quality of life with the integration of the primary sociological and secondary medical approaches. It reads as follows: "the quality of life is the adequacy of the psychosomatic state of an individual to his social status" [23].

A similar definition of the quality of life proposed by Wenger NK: the quality of life is "satisfaction from psychosocial and other forms of activity under conditions associated with illness" [24].

The Medical Encyclopedia of the Quality of Life, published in the USA, gives a simpler definition: "Quality of life is the degree of satisfaction of human needs" [25].

The author of the questionnaire of the quality of life of the hospital of St. George (SGRQ) P.W. Jones corrects the definition of quality of life from the point of view of the doctor. It sounds like "matching desires to opportunities that are limited by the disease" [26].

In modern foreign medicine, the term "quality of life related to health" is widespread, implying that there is another aspect that is not related to health: the impact of the environment, economic, political, spiritual changes. In 1982, R.M. Kaplan and Bush proposed the term "health-related quality of life" (health quality of life due to health), which made it possible to distinguish parameters describing the state of health, care for it and quality of medical care from the general concept of QOL. The concept of "health related quality of life" allows for a deep and multifaceted analysis of the physiological, psychological, emotional and social problems of a sick person [27].

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Breast cancer, biological subtypes, individual therapy for her-2 (+) (literature review)

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Abstract: The article provides an overview of the literature data on the biological subtypes of breast cancer, diagnosis and different methods of treatment depending on the subtypes.

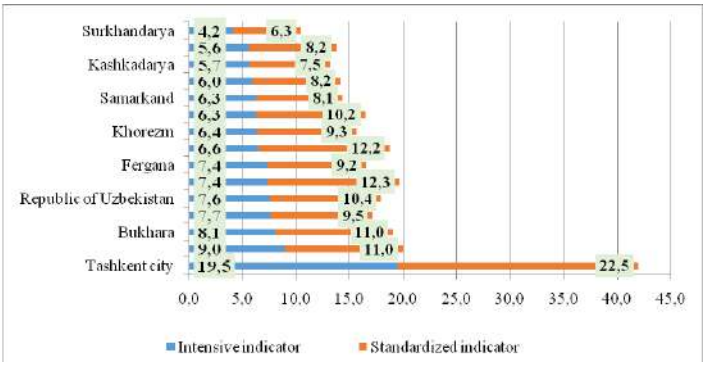
Key words: breast cancer, hormone receptor status, epidermal growth factor of a second type tumor, hormone therapy, clinical, molecularbiological criteria, phenotypes of breast carcinoma, serum concentration Her-2/neu, anti-estrogen therapy.

Breast Cancer (BC) - is one of the socially significant problems throughout the world, including in the Republic of Uzbekistan (Uzbekistan). This disease, as shown by global statistics, has a progressive growth in developing countries in comparison with economically developed countries. According to CLOBOCAN in 2012, 1 677 000 new cases were registered with this pathology, which is ? among all nosological units of malignant neoplasms (MN) [17,18]. As noted above, a high growth rate and the number of cases are also observed in developing countries, in which 883,000 cases were detected, in developed countries - 794,000 cases.

According to statistics from Russia and the CIS countries, breast cancer is in the lead, in Russia it is 18-22%, Belarus, Kazakhstan and Kyrgyzstan - 25-33%, Uzbekistan, Azerbaijan and Armenia up to 25% [3]. In the CIS countries, high standardized morbidity rates are observed in Ukraine, Belarus, Russia, and Armenia - above 40,00/0000; average - in

Azerbaijan, Turkmenistan, Kazakhstan - up to 37,00/0000; low in Tajikistan and Uzbekistan - up to 20,00/0000 [17,18].

According to scientists of Uzbekistan [11,7], the intensive morbidity rate of breast cancer in the country during the observation period from 2008 to 2010 was 7,6 per 100,000 populations, the standardized indicator is slightly higher - 13.2 (world standard). The morbidity in the regions of the republic ranges from 4,2 to 19,5. The highest morbidity is observed in Tashkent, Bukhara, Navoi cities and Tashkent regions, and low - in the Kashkadarya and Surkhandarya regions (pic. 1)



Picture 1. Intensive and standardized morbidity rates of breast cancer in Uzbekistan and its regions from 2008-2010. [11]

As can be seen from the presented data (Pic.1), there are regional features, i.e., high, medium and low morbidity rates, indicating the relevance and necessity of searching for new diagnostic methods and tactics for treating patients with this pathology. If we dwell on the mortality rates, the share of deaths from breast cancer in the republic is 20,4%, which causes the burden of breast cancer, high economic damage associated with high costs of medical examination, treatment, rehabilitation and appropriate social security.

High statistical morbidity and mortality rates dictate the need to search for conceptual approaches to the prevention and treatment of this pathology with knowledge of the modern immunological, molecular and genetic characteristics of breast cancer. The development of molecular genetic directions in the study of the occurrence of breast cancer led to the search for existing subtypes of this pathology. If we turn to history, from the end of the 20th century it became possible to determine the genetic heterogeneity of breast cancer, their origin from various morphological clones of the tumor, i.e. determination of histological types. The significance of breast epithelium stem cells mammary (MM) as a target that is subject to local and systemic effects from the early stages of carcinogenesis has been determined. In the breast during the period of pregnancy, lactation and involution,

cell lines are modified, which are formed on the basis of stem cells: 1) myoepithelial or basal (external) cells of the ducts and alveoli; 2) cells of the luminal (inner) lining of ducts; 3) alveolar cells that synthesize milk proteins. As you know, stem cells are capable of self-renewal and under the influence of hormones and stromal-epithelial interactions can actively multiply, differentiate during pregnancy and lactation, which causes a protective antitumor role of feeding, and under involution of the breast they undergo apoptosis.It turned out that some of the tumors originate from the luminal epithelium surrounding the ductal-lobular unit, and some from the basal epithelium located outwards from the luminal. Moreover, in subsequent studies, an interrelation of the origin of the tumor with clinical and prognostic characteristics, and most importantly - with a possible response to the ongoing drug therapy, was established. In the end, these factors were the real basis for revising the existing classification of breast cancer, taking into account molecular histological features [6,18]. In determining the genetic profile of the tissue and assessing the expression of biological genes, it was possible to isolate the most typical and differing among themselves, which served as the division of breast cancer subtypes into the following main ones: luminal A, luminal B, three times negative, Her-2 expressing. The division into these subtypes is based on the characteristics of the progenitor cells (luminal or basal epithelium); the presence or absence of steroid receptors and Her-2 receptors, which belong to the family of epidermal growth factors; proliferative potential; the presence or absence of cytokeratin. Each subtype of a tumor is characterized by a specific course, for example: luminal A is characterized by a good prognosis, high survival rate of patients, low recurrence rate; three times negative (TN) breast cancer - high malignancy, aggressive course, unsatisfactory response to standard therapy. Luminal B is similar to Luminous A, and Her-2 is similar to TH [6.21] with overexpression.

In the breast cells there are receptors for steroid hormones that trigger signaling pathways that regulate a number of functions - estrogen receptors (ER) and progesterone receptors (RP), they play a major role in the development of growth and metastasis of breast cancer cells. According to the Danish Breast Cancer Cooperative Group, the frequency of ER + PR + neoplasms increases with age, their characteristic decrease is observed in the range of 43-47 years. With a receptor-negative variant of the tumor (ER - PR-), they average 17.6%, increasing to 50 years. The proportion of ER + PR - subtype (13.9%) is characteristic in the initial period of menopause, subsequently slowing down, while the frequency of rarely detected ER - PR + tumors (5.6%) increases to 43-45 years with a subsequent decrease. Other authors indicate (W. Anderson et al. (2006) that intraductal, tubular and lobular carcinomas are characterized by two vertices, medullary most often occur at an average age of about 40 years, and papillary and mucinous - at 65-70 years. Comparing these observations with data on the detection of steroid hormone receptors in the same tumors, W. Anderson et al. (2006) found a certain compliance with their expectations, except for information regarding medullary carcinoma. So according to

[14,22], the group of luminal neoplasms (luminal A and B) is characterized for Caucasians in addition to steroidreceptor-positivity with an age peak of about 74 years, and the group of "basal and HER2 expressing" receptor-negative tumors is significantly different in age 50?52 years. Ethnicity was an important factor modifying both the receptor phenotype of breast tissue and the frequency of detection of individual disease subtypes. Given the existing heterogeneity of the molecular subtypes of breast cancer, the approach to the treatment of this disease should be individualized. The high cost of the necessary immuno-genetic studies limits the availability of its implementation, which leads to the conduct of therapy without taking into account tumor subtypes. Based on the existing situation, the consensus of the XIII-International Conference on Breast Cancer St.Gallen (2013) confirmed the practical suitability of the "surrogate" IHH classification of breast cancer subtypes, which includes the following options: Luminal-A, Luminal-V, HER-positive and Triple Negative.

Luminal-A - it is characterized by high expression of ER and RP, low Ki-67 (14%) and low degree of malignancy (G1-40%), favorable course, sensitivity to hormone therapy. Women who live for a long time with breast cancer have this type. It should be noted that the response to hormone therapy in this type correlates with the expression of hormone receptors, and sensitivity to chemotherapy is inversely proportional to the expression of ER. With a high content of ER and RP and a low proliferative index, hormone sensitivity and low sensitivity to chemotherapy (CT) are noted. When planning therapy for patients with luminal A subtype of breast cancer, it is necessary to take into account a positive response when using hormone therapy, while few patients need cytotoxic chemotherapy (with metastases (MTS)), i.e. hormone therapy in this category of patients is the method of choice. It is directed against the stimulating effect of estrogens on tumor cells, with the possible blocking of estrogen receptors (tamoxifen, fulvestrant) and a decrease in the level of circulating estrogens (aromatase inhibitors). In patients with locally advanced breast cancer in menopause, the use of tamoxifen or aromatase inhibitors is recommended as a neoadjuvant chemotherapy, in which the tumor can be transferred to an operable condition. With a slow flow of luminal A subtype of breast cancer of late metastases in bones, soft tissues, and lungs, several lines of hormonal therapy can be recommended, and long-term stabilization can be achieved. Tamoxifen, previously considered the first line of hormone therapy, has now given way to aromatase inhibitors in patients with menopause. A meta-analysis of 25 randomized studies comparing aromatase inhibitors and tamoxifen in patients with advanced breast cancer demonstrated the advantage of aromatase inhibitors, reducing the risk of death by 13% [4.20].

Luminal B subtype of breast cancer has a low content of RE, a lower level or negative RP, high Ki-67 (> 14%), grade of malignancy (G2-3). occurs in 30-35% of patients with breast cancer and has a less favorable prognosis compared to the luminal A subtype. It is also subdivided according to the presence or absence of HER2 overexpression / amplification. In the case of luminal B (HER2 negative) subtype of breast cancer, the treatment

tactics are similar to therapy as in the luminal A subtype, it is mandatory to evaluate the patient's condition and the presence of disease progression. With aggressive, multiple, rapidly progressing metastases, chemotherapy is preferred in the first line of therapy. After achieving a partial response or stabilization of the process, it is recommended to switch to hormone therapy, which will allow for a long time to maintain a satisfactory (8-14 months) response, prolonging life to therapy, ensuring the quality of life of the patient. It is most likely that at some point it will be necessary to appoint the next chemotherapy line, but it must be remembered that consistently using several lines of hormone therapy can delay the time of the appointment of therapy to 2 years! [4,7,9]. The use of new modern aromatase inhibitors (exemestanum in combination with the m-TOR inhibitor Everolimus) will extend the lives of patients, ensuring its satisfactory quality.

In the luminal B (HER2-positive) subtype of breast cancer, antiHER2- and hormonal therapy is used. It should be noted that overexpression / amplification of HER2 in patients with hormone-dependent breast cancer may be associated with primary resistance in hormone therapy. The basis of this phenomenon is the mutual influence of signaling pathways from HER2 and RE. In patients with HER2-positive breast cancer, the efficacy of tamoxifen was significantly lower than in HER2-negative patients (17% versus 40%), and the effectiveness of letrozole was close, i.e. these patients show resistance to tamoxifen as an estrogen receptor blocker. Inhibitors of the HER1 and HER2 receptors are recommended to be used in combination with letrozole in HER2-positive, RE-positive disseminated breast cancer.

HER2-positive (not luminal). With this subtype, HER2-positive, ER-oriented, RP-negative is detected, it is characterized by high aggressiveness, rate of progression and metastasis of both internal organs and the brain. In this regard, the determination of HER2 in primary tumors is a necessary step in the diagnosis of breast cancer, especially in aggressive and rapidly metastatic tumors. The detection of HER2 allows you to prescribe antiHER2 therapy with which you can achieve a positive clinical response and increase the life expectancy of this category of patients. One of the pharmaceutical preparations used for this type in the treatment of breast cancer is the anti-HER2 drug - trastuzumab.

Trastuzumab (Herceptin) - refers to humanized monoclonal antibodies that selectively bind to Her-2 / neu receptors, the main mechanism of which is to accelerate the degradation of the HER2 receptor proteins, which mobilize immune cells to destroy tumor target cells with the manifestation of anti-dependent cell-mediated cytotoxicity, concentrations of endothelial growth factor and other angiogenic effects. This drug should be administered only if there is a Her-2 / neu receptor overexpression, which is determined using the immunohistochemical method (IHH) (grades from 0 to 3+) and the fluorescent in situ hybridization method (FISH) (expensive, but more accurate)) [2,7]. The most frequent (up to 40%) side effects of treatment with trastuzumab are infusion reactions in the form of fever and chills, characteristic of the first injection of the drug. One of the serious toxic effects are dysfunction of the heart

(4.7%), while more than 1% of patients need to stop using the drug [2.8]. In patients with IHC 2+ status, FISH should be performed, and only with FISH positive tumors, treatment with trastuzumab is recommended.

Most often, trastuzumab is used in combination with taxanes. Trastuzumab increases the antitumor efficacy of chemotherapy with anthracyclines, taxanes, vinorelbine, capecitabine, platinum preparations, gemcitabine. Combinations of anthracyclines and trastuzumab have high antitumor activity, but the simultaneous use of trastuzumab with anthracyclines is not recommended, as they have cardiotoxicity, which, unlike trastuzumab, is cumulative and irreversible. Currently, it is considered appropriate to continue monotherapy after the first line of chemotherapy in combination with trastuzumab. It is advisable that with the progression of breast cancer continue the introduction of anti-HER2 and change the chemotherapy regimen, as part of the tumor clones retains sensitivity to it, and it in turn has a synergistic effect with cytostatics. Combinations, including anthracyclines and taxanes, are widely used in the first line therapy of breast cancer and in operable forms as an adjuvant and neoadjuvant XT. According to the results of the largest study (HERA), the introduction of trastuzumab into the adjuvant therapy regimens will allow a 2.5% reduction in the number of patients who develop distant metastases after "radical" treatment, which will be 27,727 women for five European countries [2, five]. A number of issues relating to the clinical use of trastuzumab, continues to be actively studied in the present. There is evidence of the continued efficacy of the drug in the treatment of metastatic cancer even after the progression of the tumor process (currently, it is recommended to continue anti-Her-2 therapy with a change in the mode of "classical" chemotherapy).

Triple negative breast cancer - characterized by a negative-re, RP, HER2-negative.Triple negative subtype is detected in 15-20% of patients with poor prognosis. Its incidence in young patients is depressing, the rapid rate of tumor growth and metastasis, a high degree of malignancy (G3), high Ki-67, early progression, sensitivity to chemotherapy, low survival. With this subtype of breast cancer, anthracyclines, taxanes, and their combinations are effective. Given the high proliferative activity of this subtype of breast cancer, its high sensitivity to chemotherapy is characteristic. About 10% of triple negative breast cancer is BRCA1-associated. In young women with atriple negative subtype of breast cancer, it is necessary to determine the BRCA1 mutational status, since the presence of a triple negative breast cancer in apatient younger than 50 years increases the chance of finding a BRCA1 mutation 10 times. In BRCA1-associated breast cancer, cytostatics are effective, which interfere with DNA synthesis, including platinum derivatives.

With the rapid development of metastases and their threat, it is necessary to think first of all about the luminal A and B subtypes. So, with HER2 positive breast cancer, a combination of antiHER2 and cytostatic is recommended, and with triple negative breast cancer - only chemotherapy, the luminal-A subtype is preferable to use hormone therapy, therapy with bisphosphonates, as indicated by local radiation therapy.

Thus, chemotherapy for breast cancer must be "individualized", taking into account and determining the subtypes of breast cancer and the hormonal status of each patient.

A more accurate molecular genetic characterization of clinical subtypes of breast cancer will facilitate adequate therapy, which in turn will give a satisfactory clinical effect.

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Prevalence Of Major Salivary Gland Tumors At Almouasat University Hospital

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Abstract: Objective: this study aimed to study the prevalence and incidence of Salivary gland tumors. Materials and Methods: This is a retrospective study of salivary gland tumors diagnosed between 1/1/2014 to 30/7/2018 from AlMouasat University Hospital records.Results: This study consisted of 72 cases. Most of them were benign tumors 79.2%. Parotid gland was the most affected. Pleomorphic adenoma 43.1% of and squamous cell carcinoma 6.9% were the most common benign and malignant tumors, respectively. Conclusion:Salivary gland neoplasms are not common. Most common gland in which tumors rise is the parotid gland. Pleomorphic adenoma of and squamous cell carcinoma were the most common benign and malignant tumors, respectively.

Key words: Salivary, gland tumors, respectively, Almouasat university hospital

Introduction:

Salivary gland neoplasms (SGNs) composes a diverse group of tumors. This diversity makes the diagnosis and management of these tumors quite troublesome for the surgeon or the pathologist. (1).

SGNs are not common and their incidence is between 0.4-13.5 cases per 100,000 population. (2). Malignant SGNs accounts for 3-6% of all head and neck cancers and composes around 0.5% of all malignances. Hence, salivary gland malignances are rare.

The main challenge in these tumors is that their histopathology is the most complex of any organ or tissue. (3) Benign SGNs are more common in clinical practice with 5-7 more times than their malignant counterparts.

Parotid and submandibular glands are the most affected glands, respectively. Most of SGNs are benign tumors.

Up to our knowledge, this study is the first of its type in Syria.

Materials and Methods:

This study was a retrospective study of the records of the patients who reviewed AlMouasat University Hospital with salivary gland tumors.

We studied the demographic variables of these tumors, such as age and gender. We studies the prevalence of different types of tumors and their correlation with age and gender.

This study included all cases from 1/1/2014 to 30/7/2018. Only the authors to ensure the privacy collected all the data to ensure the privacy and all the names and personal information were blinded. Statistical analysis was done using SPSS 25.0.

Results:

Table 1: Demographic variables of our study and the distribution of tumors in the glands.

Variable		frequency	percent	total
Age	0-10 year	1	1.4	72(100%)
	11-20 year	3	4.2	
	21-30 year	9	12.5	
	31-40 year	13	18.1	
	41-50 year	17	23.6	
	51-60 year	11	15.3	
	61-70 year	10	13.9	
	71-80 year	7	9.7	
	81-90 year	1	1.4	
Gender	Male	29	40.3	72(100%)
	Female	43	59.7	
Gland	Parotid	67	93.1	72(100%)
	Submandibular	5	6.9	

Table 2: Types of tumors in our study:

		N	%
Malignancy	Benign	57	79.2
	Malignant	15	20.8
	Total	72	100.0

Table 3: Distribution of tumors in our study:

			N	%	% of all sample
Tumor types	**Benign**	Warthin's Tumor	21	36.8	29.2
		Myoepitheioma	1	1.8	1.4
		Oncocytoma	4	7.0	5.6
		Pleomorphic adenoma (PA)	31	54.4	43.1
		Total	57	100.0	-
	Malignant	Mucoepidermoid Carcinoma (MEC)	4	26.7	5.6
		Adenoid Cystic Carcinoma (ACC)	4	26.7	5.6
		Myoepithelial Carcinoma	1	6.7	1.4
		Clear Cell Adenocarcinoma	1	6.7	1.4
		Squamous Cell Carcinoma	5	33.3	6.9
		Total	15	100.0	100.0

Table 4: Distribution of all tumors in correlation to gender:

						Chi-Square test	
			Gender		Total	Chi-Square	p-value
			Male	Female			
Type	Warthin's Tumor	Count	15	6	21	18.655	0.000*
		% of Total	20.8%	8.3%	29.2%		
	Myoepitheioma	Count	0	1	1		
		% of Total	0.0%	1.4%	1.4%		
	Oncocytoma	Count	3	1	4		
		% of Total	4.2%	1.4%	5.6%		
	PA	Count	5	26	31		
		% of Total	6.9%	36.1%	43.1%		
	MEC	Count	2	2	4	1.667	0.797
		% of Total	2.8%	2.8%	5.6%		
	ACC	Count	2	2	4		
		% of Total	2.8%	2.8%	5.6%		
	Myoepithelial Carcinoma	Count	0	1	1		
		% of Total	0.0%	1.4%	1.4%		
	Clear Cell Adenocarcinoma	Count	0	1	1		
		% of Total	0.0%	1.4%	1.4%		
	SCC	Count	2	3	5		
		% of Total	2.8%	4.2%	6.9%		
	Total	Count	29	43	72		
		% of Total	40.3%	59.7%	100.0%		

The correlation between malignant tumors and age was not statistically significant ($p > 0.05$) so their results were not shown.

Table 5: Distribution of all tumors in correlation to age:

			Type					Chi-Square test	
			Warthin Tumor	Myoepitheloma	Oncocytoma	PA	Total	Chi-Square	p-value
Age	0-10 year	Count	0	0	1	0	1	42.534	0.004*
		% of Total	0.0%	0.0%	1.8%	0.0%	1.8%		
	11-20 year	Count	0	0	0	2	2		
		% of Total	0.0%	0.0%	0.0%	3.5%	3.5%		
	21-30 year	Count	1	0	0	8	9		
		% of Total	1.8%	0.0%	0.0%	14.0%	15.8%		
	31-40 year	Count	0	1	1	8	10		
		% of Total	0.0%	1.8%	1.8%	14.0%	17.5%		
	41-50 year	Count	6	0	0	9	15		
		% of Total	10.5%	0.0%	0.0%	15.8%	26.3%		
	51-60 year	Count	7	0	1	2	10		
		% of Total	12.3%	0.0%	1.8%	3.5%	17.5%		
	61-70 year	Count	4	0	1	2	7		
		% of Total	7.0%	0.0%	1.8%	3.5%	12.3%		
	71-80 year	Count	3	0	0	0	3		
		% of Total	5.3%	0.0%	0.0%	0.0%	5.3%		
Total		Count	21	1	4	31	57		
		% of Total	36.8%	1.8%	7.0%	54.4%	100.0%		

Discussion:

SGNs as a whole are more common in females according to the WHO (World Health Organization) and other articles (4, 5). However, some studies states that these tumors has a men predominance. (3, 6, 7, 8). In our study, we had 72 patients of which 43 of them were females (59.7%) and 29 were males (40.3%). (Table 1)

Similar studies shows that the prevalence of benign and malignant was 70.3% and 29.7%, respectively. Chili study. Moreover, a Brazilian study showed a prevalence of 74.8% benign and 25.2%. (5, 6). In our study, the results were similar to literature; we had 79.2% benign and 20.8% malignant. (Table 2)

Two similar studies (5, 10) showed that the most common gland for salivary neoplasms was the parotid gland. In our study, the neoplasm benign or malignant were found either in the parotid gland (most common, 93.1%), and in the submandibular gland (6.9%). (Table 1)

The most common benign tumor in ourstudy was pleomorphic adenoma followed by Warthin tumor, while the most common malignant tumor was squamous cell carcinoma compared to similar studies (10) in which the mucoepidermoid carcinoma was the most common. (Table 3)

Most of the pleomorphic adenomas were found in females, which is concordant to similar studies (5, 10, 11). Warthin tumor was predominant in males, which has been stated in other literature. (5-6, 9, 11). Squamous cell

carcinomas were more common in females in our study; however, we could not find any studies that discuss the gender predominance of malignant salivary gland tumors.(Table 4)

The average age of presentation of SGNs was 53.3 years in a similar study (10). In our study, there was a statistical correlation between the age and benign tumor types ($p<0.05$). The peak incidence was 41-50 years old. The two most prevalent benign tumors Pleomorphic adenoma and Warthin tumor was most common between 41-50 years old and 51-60 years old, respectively. It should be noted that the risk of salivary gland cancer increases with age (12). We did not find a statistical correlation between the age and malignant tumor types ($p>0.05$). Nevertheless, the most common malignant tumor Squamous cell carcinoma was most common between 61-70 years old. It should be noted that 8 out of 15 cases of malignances was in patients between 61-90 years old.(Table 5)

Conclusion:

Salivary gland tumors are uncommon neoplasms that usually arise in the parotid gland showing some predilection for females. Benign tumors are by far more common than malignant tumors. Pleomorphic adenoma and squamous cell carcinoma were the most common benign and malignant tumors reported in this series, respectively.

Compliance with Ethical Standards:

Funding: This study was not funded by any institution.

Conflict of Interest: The authors of this study have no conflict of interests regarding the publication of this article. Ethical approval: The names and personal details of the participants were blinded to ensure privacy.

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Hygienic Assessment Of The Use Of Plant Raw Materials In The Production Of Meat Products

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Abstract: In Uzbekistan special relevance gets uses in production of meat products, products of processing of grain which are a source of food fibers and promoting increase in body resistance of the person to harmful effects of the environment. It is known that flour from grain of groat cultures (rice, a buckwheat, a millet, oats, barley, etc.) has more valuable properties in comparison with flour from traditional grain cultures. One of the most popular around the world and the second culture on the output grain is grain from rice. Rice grain contains full-fledged protein, starch, has high ability to swelling. At rice flour there is a silicon promoting processes of a metabolism in a human body. Besides, it contains rather large amount of biotin and also other microelements having important medicobiological value. For assessment of quality of rice flour its chemical composition and functional and technology properties were studied. Also the expediency of use of rice flour of different types of processing for production of meat products was considered.

Keywords: Sausages, beef meat, fillers, rice flour, wheat flour.

Introduction According to the FAO / WHO, by 2050, the world's population will reach 9.1 billion people, 34% more than today. In order to feed this growing, more urbanized population, which is more prosperous, food production must increase by 70%. Thus, annual grain production should reach 3 billion tons compared with the current 2.1 billion, and annual meat production should grow by more than 200 million tons and reach 470 million tons (1). Thus, the maximum use of alternative products in comparison with existing ones becomes even more important and relevant. The meat industry is one of the largest sectors of the food industry, it is designed to provide the population with food products, which are the main source of proteins. Meat products are agri-food products of animal origin.

It is known that for the normal functioning of the human body in the diet it must contain sets of essential amino acids, most of which supply meat products.

The necessary conditions for increasing the volume of production of meat products and improving their quality are improving the efficiency of using raw materials, reducing losses and improving the range of products. Of particular relevance is the ability to use in the composition of meat products of cereals, subjected to various methods of modification, due to their high nutritional value and functional and technological properties.

Domestic and foreign scientists (Zharinov A.I., Zhuravskaya N.K., Lipatov N.N., Lisitsyn A.B., Pokrovsky A.A., Rogov I.A., Titov E.I., Tolstoguzov V. B., Salavatulina RM, Feys M., Arnaut F., Mittal GS, Kady A., Welz W., Hand Z., etc.) showed the feasibility of creating combined meat products, including vegetable components and having high consumer properties. Analysis of the properties of rice flour subjected to various types of processing and the creation of meat products using it will reduce the existing protein deficiency, reduce production costs and increase the volume of products that meet modern requirements of the science of nutrition, and make rational use of meat raw materials.

Purpose: Hygienic assessment of the influence of technological factors on changes in the chemical composition of plant materials and the safety of finished products according to sanitary and hygienic indicators.

Results and its discussion. The production of high-quality meat products is a complex task. Its solution depends on the improvement of integrated and waste-free technologies for the processing of agricultural raw materials, further automation and mechanization of agriculture and processing industries, reduction of raw materials, energy and labor costs.

Today the market of sausage and gourmet products is one of the largest and most dynamic markets for food products. It has very strong traditions, and its condition has a significant impact on other food markets. It is characterized by a higher level of competition, and in this area small private production and well-known manufacturers with big names work. Sausage can be considered a kind of barometer of the welfare of the population. In times of stability and improvement in the economic situation, the consumption of sausages increases; if the financial situation of the population deteriorates, then the demand for sausage decreases. The range of sausage products produced is expanding, production volumes of products that are in high demand among the population are growing. Today, on the shelves of retailers you can find a considerable amount of sausage products in attractive packaging. In each outlet, sausages, sausages, smoked meat are presented in a wide range by a large number of producers. At the sight of such a variety, it is difficult for an ordinary buyer to make a choice. And here the company's brand plays a big role. The production of sausages is one of the primary places in the food industry. But the manufacturing technology of gastronomic products is quite complex, it requires the use of special equipment and a high level of personnel training. The leading company LLC MasterDelikatesov contributes to the development of the domestic food industry and the saturation of the food market.

One of the main tasks for developers of new types of meat products is to obtain

products with a set of specified useful properties and having high consumer qualities. The use of plant materials in the production of meat products allows not only to enrich them with biologically active substances, but also to normalize the acidity in the human body, to increase the digestibility of these products.

In recent years, in many countries in the production of meat products used plant materials. In Uzbekistan, the possibility of using cereals in meat products is of particular relevance due to their high nutritional value and functional and technological properties. These cultures are a source of dietary fiber (PV) and significantly contribute to increasing the resilience of the human body to the harmful effects of the environment. Grain contains almost all the basic substances necessary for normal human life. It is known that flour from grain of cereals (rice, buckwheat, millet, oats, barley, etc.) has more valuable physiological and biochemical properties compared to flour from traditional cereals. Flour of grain crops is rich in the content of the most valuable natural components, including amino acids, certain vitamins, microelements (calcium, phosphorus, iron, iodine), as well as beta-glucan, which reduces the level of cholesterol. One of the most popular worldwide and the second crop in terms of cereal production is rice cereals. Rice grain contains high-grade protein (7-10%), starch (66-70%), has a high ability to swell. Silicon is present in rice flour, contributing to metabolic processes in the human body. In addition, it contains a relatively large amount of biotin, as well as other trace elements that have important medico-biological significance. To assess the quality of rice flour, its chemical composition and functional and technological properties were studied: water binding capacity (BCC), fat binding capacity (LSC), emulsion stability, gelation ability. The expediency of using rice flour of various types of processing (fine grinding, IR processing, processing by thermoplastic extrusion) for the production of meat products was also considered.

Rice flour "extra" is a natural product containing a large range of natural trace elements, vitamins and minerals that have high biological value. From the point of view of meat production technology, rice flour has the following advantages:

- Can be added to raw meat, both dry and hydrated;
- Binds water in a ratio of 1: 4-1: 4,5;
- Reduces the loss of raw meat during its heat treatment;
- Increases juiciness;
- Has a neutral taste;
- Has a high nutritional value;
- Forms stable gels;
- The water-holding capacity of rice flour: in the production of chopped semi-finished products, including dumplings, 100%; in the production of sausages - 600%; 180% Giro retention.

There is no fat in rice flour (as opposed to soy flour and soy isolate), which allows meat products to retain the inherent taste after heat treatment.

One of the ways to improve the quality of products and improve the structure of nutrition of the population is the introduction of new non-traditional types of plant materials into the diet. Created products must contain a balanced complex of proteins, lipids, minerals, vitamins, ballast substances and have high nutritional and taste properties.

In recent years, the range of meat products has significantly expanded, in

the recipe of which various ingredients of non-meat origin are used. Studies by Russian and foreign authors have shown the promising use of grain processing products in the technology of combined meat products, which provide high nutritional and biological value of the product, help to increase the flexibility of recipes, stable and even distribution of ingredients, minimize losses in the production process, which ultimately leads to creating a product of stable quality.

In world practice, considerable experience has been gained in the use of grain products in the manufacture of combined products.

Many nations have historically developed the tradition of using meat in combination with flour products (dumplings, pies, manti, pasties, etc.). Possessing a complete set of essential amino acids, meat proteins significantly increase the amino acid fastness of grain products and, accordingly, their digestibility. This is particularly important, since the cereal proteins are not completely absorbed by the body, for example, wheat proteins - only by 69%.

The current technology of minced products involves the use of various starch-containing raw materials, which contributes to some increase in the moisture and fat-binding capacity of the stuffing system. Traditionally, sausage production uses wheat flour, starch and cereals (millet, rice, barley, barley, etc.). Wheat flour and starch are widely used in small quantities (2-3%) to increase the viscosity and water-holding capacity of minced boiled, liver and other types of sausages. The meat industry of the Republic of Uzbekistan has developed a range of semi-smoked sausages using from 2 to 5% wheat, rice, barley or oatmeal, as well as a wide range of boiled sausages, sausages and wieners using hydrated cereals (barley, oatmeal, pea flour) in quantities up to 15 % instead of raw meat. Products are characterized by stable quality and high consumer properties.In the same amount, starch and wheat flour are included in the recipe for chopped ham products (75). Herbal ingredients are increasingly used as a partial or complete replacement of meat in various products, previously produced only from raw meat. An example would be meatballs, which include 60% of meat and up to 5% of "wheat fibers". Studied the use of herbal supplements through a combination of protein, lipid and mineral components. As a result of the use of compositions with legumes, the biological value of sausages is increased by 19-20%, and the energy value - by 3-5%. The possibility of dry powders from pumpkin, carrots, beets, eggplants, apples, tomatoes and other vegetable crops in the production of boiled sausage is also shown.

The increasing interest of science and industry is caused by the use of ecologically safe plant raw materials in the production of food products and therapeutic and prophylactic preparations made from local raw materials. Food products made from local raw materials have the best therapeutic effect for people living in the relevant area. Such products increase the body's resistance to extreme situations, normalize mental and physical performance.

The Ministry of Health of the Republic of Uzbekistan recommends that manufacturing enterprises abandon the use of modified (with a modified gene structure) products. Recent scientific studies have shown that these products are unsafe for the health of people,

especially children. Unlike genetically modified additives, often used in meat production, rice flour is a natural product containing a large range of natural microelements, vitamins and minerals of high biological value. Data on the chemical composition of rice flour are presented in the tables.

Table 1. Nutritional value

Name	Proteins, gr	Fats, gr	Water, gr	Alkali, gr	Carbohydrate, gr	Caloric Value, ccal
Beef	18,6	16	69,6	1	0	218
Cooking Salt	-	-	0,2	9		0
Rice flour	8	1			81	345

Table 2. Vitamincomposition

Name	PP, mg	B1,mg	B2,mg	B3,mg	B6,mg	B9,mcg	E, mg	Choline, mg
Beef	4,7	0,06	0,2	0,5	0,4	8,4	0,6	70
Rice flour	2	0,7	0,2	-	-	-	2,5	-

Table 3. Macro and micro elements

Name	Macroelements, mg							Microelements, mcg								
	Ca	Mg	Na	K	P	Cl	S	Fe, мг	Zn, mg	J	Cu	Mn	Cr	F	Mo	Co	Ni
Beef	9	22	65	325	188	59	230	2,7	3,24	7,2	182	0,035	8,2	63	11,6	3	-
Cooking Salt	368	2,9	368	22	-	59690	180	2,9	6600	-	271	250	-	-	110	15	-

Table 4. Amino acid composition

Factors	Beef	Rice flour
Essential Amino Acid		
Valine	790	996
Isoleucine	730	799
Leucine	1750	1494
Lysine	2010	1739
Methionine	420	473
Threonine	1260	923
Tryptophan	198	282
Phenylalanine	860	857
Nonessential amino acid		
Alanine	1230	1033
Arginine	1570	1395
Asparagi(ni)c acid	1442	1909
Histidine	990	820
Glycine	920	861
Glutami(ni)c acid	2459	2941
Proline	741	923
Serine	750	869
Tyrosine	640	687
Cystine	200	301
The total number of amino acids	18960	19302

Conclusion

Thus, unlike the genetically modified additives often used in meat production, rice flour is a natural product. Rice flour is recommended to be used as an additive in the production of meat products such as: cooked sausages, cooked smoked sausages; semi-smoked sausages; sausages, sausages; dumplings; meatballs; meatballs; meatballs; liver pates; pastry fillings. Rice flour not only superbly replaces native and chemically modified starches, concentrates and isolates of soy proteins and their modified preparations, exceeding its cost, but also increases the yield of finished products, reduces thermal loss and does not change the protein content in the final product, giving the products a pleasant taste and appearance.

The quantity and quality of the meat product depends on the physicochemical properties of the constituent components of the raw meat, the ability of these components to intermolecular interaction, as well as the retention of moisture by protein substances during cold processing of meat and subsequent thermal effects. In the case when a high content of free moisture in meat products is undesirable and it is required to strengthen the connection between its

components, add rice flour to the raw meat. In the process of heat treatment of raw meat, with the introduction of rice flour, there is a gelatinization of the polysaccharides contained in it (amylopectin and amylose), which, when interacting with other components, retain moisture, forming a colloidal dispersion. At the same time, rice flour polysaccharides not only retain free moisture, but interact with protein molecules of raw meat, which allows to improve its structure and facilitate further work on its formation (it is important in the production of sausages). Rice flour is hydrated and added instead of raw meat, which will allow, in addition to the properties described above, to obtain additional output of finished meat products and lead to cost reduction. The optimal addition of rice flour is 10% by weight of raw meat. The amount of water can vary depending on the formulation used in the enterprise. There is no fat in rice flour (as opposed to soy flour and soy isolate), which allows meat products to retain the inherent taste after heat treatment.

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Some Immunity Indicators In Patients With Chronic Obstructive Pulmonary Disease

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Abstract: The basic foci of inflammation inchronic obstructive pulmonary disease in small airways; however, active inflammation also developsinthe large bronchial tubes, pulmonary parenchyma, and pulmonary vessels. During the conducted research eightyCOPD patients wereincluded on in the research, among them 51patients were males (63.7 %) and 29 were females (36.3 %). Severity of COPDgrade 1 diagnosed in 25 patients, grade П -in 28 and grade Ш -in 27 patients. According to reached results of research, an increase in the leukocytes and lymphocytes levelsoccurredinCOPD patients. As the findings of our research, demonstrate that the relative level of CD95 + lymphocytesturned to beincreased in severe COPD in comparison with other groups of the involved patients. Also, the rising of some pro-inflammatory (IL-1 ?, IL-1 ?, IL-8, the TNF?, IFN?) and depression of anti-inflammatory cytokines (IL-4) has been taped in a blood of patients with COPD at advance of this disease.

Key words: chronic obstructive pulmonary disease, immune system,lymphocytes,cytokines.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a serious medical and social problemworldwide [1]. An essential rolein COPD development is plaid byimmune-reactivityof a whole body and local protective factors in the lungs. At early stages of the disease,the inflammatory process, which is the caused by inhalation of tobacco smoke, can be reversible. However,in the course of time the inflammation of the airways becomes chronic and persists even after the smoking cessation.The basic foci of inflammation inCOPD are small airways; however, active inflammation also developsinthe large bronchial tubes, pulmonary parenchyma, and pulmonary vessels [3, 4, 5]. One of COPDmanifestations is systemic inflammation of the body shown by changes in the immune system [6,7]. Several studies demonstrated the presence of high levels of inflammatory cytokines and other mediators in thelungs and bronchoalveolar lavage fluid of COPD

patientsas well as in their blood [8, 9, 10]. Still the mechanisms of interrelation of the systemic and local inflammation inCOPDrequire further studying.

In this connection, the objective of our research was to study thesome of the indicatorsof cellular immunity and the cytokine profile inpatients with chronic obstructive pulmonary disease depending on severity of the disease.

MATERIALS AND METHODS.

EightyCOPD patients wereincluded on in the research, among themwere 51 males (63.7 %) and 29 females (36.3 %). COPDwith severityof 1 gradewas diagnosed in 25 patients, grade П -in 28 and grade Ш -in 27 patients. The diagnosis of chronic obstructive pulmonary diseasemadebased on the criteria stated in theGOLD program "Global strategy for diagnosis, management, andprevention of chronic obstructive pulmonary disease"[2].The control group consisted of 20 people with no signs of diseases of the respiratory and immune systems. The mean age of the patients was 47ë1.5 years with the disease duration ranged from 3 to 15 years. The analysis of the lymphocyte subpopulations made with monoclonal antibodies of LT series (the Scientific Centre of the Institute forImmunology). The percentage of the general population of cells expressing CD3 +, CD4 +, CD8 +, CD16 +,CD95 + markers and HLA-DR + lymphocyteswas calculated. Simultaneously, the clinical analysis of blood was made to get the absolute quantity of the cells (Dahl R., 1993). To evaluate theneutrophilsstatus in the peripheral blood the latex produced by theInstitute of Biological Instrument Manufacture (Russia)was used.Levels of cytokines IL-1 ?, IL-1 ?, IL-4, IL-8, TNF?, IFN? in blood serum defined with the help of hard - fazed enzyme immunoassay analysis.

RESEARCH AND RESULTS

As the research results have shown, an increase in the leukocytes and lymphocytes levelsoccurredinCOPD patients. The absolute level of cells expressing CD3 + marker in the patientswith COPD of mild severity is within the normal limits. Inmoderate and severe COPD, this indicator has raised. A reliable decrease in the percentage correlation of cells expressing CD3 + marker was observed at all COPD severity levels. In our opinion, an increase in CD3 + lymphocytes in the patients' blood suggest their insufficient migration to the inflammation focus in the airways that means a sign of poorprognosis. A reliable decrease was observed in the absolute and relative numbersof lymphocytesexpressing CD4 + marker in all the COPD patients, that indicates the intensity of cellular immunity inCOPD and a decrease in proliferation and differentiation ofB-lymphocytes.In addition,the disbalance was observed in the value of CD4 +/CD8 + marker of immunity regulation: this indicator was dramatically decreased at all COPD severity levels.

The conducted researches have shown that at COPD at an easy current level interleukin IL-8, has appeared to be raised in 1,4 times, at COPD of moderately severe level - in 4,1 times, at COPD with a serious current - in 5,5 times. Concentration of IFN? in comparison with control was lowered in 1,2 times at the second degree of COPD and enlarged more than in 1,5 times at the third stage. Action of IFN ? promotes development of effective remedies of return regulation

of its activity in particular in the form of an anti-inflammatory cytokine, for example of interleukin-4. IL-4 was produced by Th2 subpopulation of lymphocytes, stimulates a proliferation and a differentiation of V-cages and synthesis IgE, and inhibits production of inflammatory cytokines. [10]. At patients the level of IL-4 at easy current of COPD has appeared raised almost in 3 times, at average - in 2 times, and at COPD a serious current - in 1,5 times in comparison with control. It known that on activity of IL-1 ? it is possible to judge synchronization of inflammatory process at COPD. So, level of IL-1? was lowered at COPD an easy current - in 5,1 times, at COPD of middle-hard current - in 6,1 times, at serious COPD - in 3,2 times in comparison with control group. Concentration of TNF? has appeared to be lowered at COPD of an easy current in 1,5 times, at COPD of moderately severe level - in 1,27 times whereas, on the contrary, at COPD of a serious current this indicator has appeared raised almost in 3 times.

Table 1

Some immunologic indicators of COPD patients

Indicators	COPDI (n=25)	COPD II (n=28)	COPDIII (n=27)	Control group (n=20)
Leucocytes, absolute number	6.5±6.32	7.67±0.55*	8,93±0.85*	5.51±0.21
Lymphocytes,%	25.08±2.2	31.53±1.1*	39.4±2.1*	24.30±1.2
Lymphocytes, absolute number	2.28±0.32	2.50±0.11	2.76±0.16	2.33±0.21
CD3+, absolute number	1.46±0.11	1.66±0.22	1.82±0.09	1.62±0.14
CD3+, %	68.61±0.52*	66.42±0.98*	60.78±1.11*	72.31±2.21
CD4+, absolute number	0.86±0.05*	0.86±0.09*	0.91±0.11*	1.31±0.12
CD4+ %	41.51±0.85*	42,23±1.01*	41.75±0.98*	46.18±1.20
CD8+,absolute number	0.61±0.04	0.62±0.03	0.78±0.01*	0.60±0.02
CD8+, %	33.32±2.41	34.00±1.81*	41.88±2.26*	26.98±1.24
CD16+.absolute number	0.21±0.0001	0.22±0.002	0.22±0.002	0.21±0.001
CD16+, %	18.67±0.31*	18.44±0.35*	18.56±0.42*	16.86±0.36
CD95+,absolute number	0.21±0.015	0.21±0.004	0.22±0.002	0.21±0.003
CD95+, %	10.84±0.29	11.88±0.23	12.94±0.44	11.26±0.56

*Reference: * - p<0,05 in comparison with control*

Table2.

Consistence of interleukins in blood of patients with COPD

Interleukins	COPDI (n=25)	COPD II (n=28)	COPDIII (n=27)	Control group (n=20)
IL-8 pg/ml	22,34±2,48	62,44±4,01*	86,36±3,22*	14,78±1,48
IL-1α, pg/ml	8,57±1,21	7,62±1,02	21,08±1,52	0
IL-1β, pg/ml	6,39±1,04*	5,34±0,98*	9,75±1,11*	31,71±2,02
IFNγ, pg/ml	189,61±4,04	148,12±5,01*	305,08±4,02*	192,64±3,42
FNOα, pg/ml	32,00±2,98	40,48±4,01	135,42±3,48*	47,12±2,52
IL-4, pg/ml	78,61±4,42*	51,10±3,35*	34,66±2,02*	25,53±1,78

*Reference: * - p<0,05in comparison with control*

DISCUSSION

Reliably increased relative level of CD16+ lymphocyteswas at allCOPD severity levels. It is known that one of CD16 + lymphocytesfunctionsto be participation in antineoplastic immunity; therefore,the patients demonstratedthe intensityof the protective killer functions of lymphocytesassociated with possible development of oncological processes against the background of pathomorphologicalprocesses inCOPD. As the findings of our research demonstrated,the relative level of CD95 + lymphocytesturned to beincreased insevere COPD in comparison with other groups of the involved patients.

IL-8 is produce by monocytes and macrophages, carries out a role of an inductor of acute inflammatory reactions. Rising of level of IL-8 at advance COPD can speak that intensive and long inflammatory processes was accompanied by accumulation in a blood of proinflammatory cytokines. Low maintenance of IFN? at COPD of an easy current, and its deficiency at COPD of middle-hard current can testify the insufficient efficiency of cellular factors of immunity. Raised maintenance of IFN? at the third group of patients with COPD can testify the more expressed antigenic stimulation and the prevalence of the cellular-mediated immune answer at a serious current of disease. Occurrence of IL-1? testifies to damage of cells of an epithelium of a mucosa of bronchus, as it is an intracellular cytokine. Low sizes of TNF? at a lung and middle-hard current of COPD should treated as the indicator of insufficient stimulation of macrophage organism protection. Obviously, raised maintenance of TNF? at COPD of a serious current are cause by development

of an inflammation and a cellular destruction of tissues.

Thus, at patients with COPD change of cytokine profile was tape irrespective of a disease stage. Expression of these changes depends on gravity of COPD and define degree of a system inflammation in an organism, which can in its turn, immediate influence the forecast and outcome of COPD. Cellular factors of immunity inCOPD at various stages waslinked with alterationsin the levels of leukocytes andlymphocytes, a decrease in CD3 +, CD 4 +, CD 16 + cells.The degree of expression ofimmunologic disorders of the cellular link of the immune system directly depends on COPD severity and determines the disease prognosis.

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