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# Section 1 Original articles

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# NON-MOTOR VISUAL DISORDERS IN KAZAKHTAN PATIENTS WITH PARKINSON'S DISEASE

We observed 106 Parkinson's patients in Almaty city to detect non-motor visual disorders.

Among non-motor symptoms in patients with Parkinson's disease (PD), visual symptoms are becoming increasingly important. Visual impairments cause severe disability, reduce compensatory ability and adaptation of the patient to motor impairments and reduce life expectancy. Many neurologists do not take into serious consideration the importance of visual disorders in PD. This type of research has never been carried out in Kazakhstan or indeed the rest of Central Asia.

To study visual non-motor disorders in PD patients in Almaty to help optimize diagnosis and evaluate their correlation with disease duration and severity.

The diagnosis included the following elements: patient's complaints and history, a general physical examination, a neurological examination with auxiliary assessment scales.

The study confirmed that non-motor manifestations are common in PD patients. Research to date has confirmed the predictive value of non-motor PD manifestations.

Non-motor visual impairments are important to the overall quality of life of Parkinson's patients as well its motor manifestation, and require a very careful approach and considerable effort for early detection by a physician, medical personnel and caregivers, including relatives.

Key words: Parkinson's Disease, non-motor manifestations, clinical features, MDS(UPDRS), Kazakhstan.

# Introduction

According to Global Burden of Disease 2016 6,1 million people in the world suffer with Parkinson's disease, out of which 2,9 million (47,5%) are women and 3,2 million (52,5%) are men [1]. The projected increase in the number of patients over the next 30 years will result in more than 12 million patients worldwide by about 2050 [1,2].

Parkinson's disease (PD) is characterized by a number of classic motor symptoms, including tremor at rest, rigidity and bradykinesia, which occur in the early stages of the disease and are highly dependent on neuronal degeneration of dopaminergic neurons from the substantia nigra pars compacta [3]. However, PD symptoms are now recognized as heterogeneous, with clinically significant non-motor features such as cognitive disorders, autonomic dysfunction, neuropsychological symptoms, sleep disorders, pain, fatigue and olfactory dysfunction, aggravating the disability. There is increasing evidence that non-motor PD symptoms do not only occur at an early stage of the disease, but may also precede motor symptoms by several years [4].

The prevalence of PD patients in Kazakhstan averages 62 cases per 100,000 and increases significantly above 70 years of age, with the average age of onset being 56.4  $\pm$ 2.8 for women and 63.3  $\pm$ 3.5 for men [5,6]. Various studies have shown that the disease manifests when 50% to 70% of substantia

nigra neurons die and dopamine levels in the striatum are reduced by more than 80% [7,8,9,10].

Braak H, et all (2004) have expressed the opinion that long before the characteristic clinical motor symptoms of PD appear, the pathological process begins from the vagus nerve to the brain stem and eventually progresses to the limbic and neocortical regions of the brain [9]. This determines the development of various non-motor and premotor clinical manifestations of PD – sensory, vegetative, dissimilar, affective, etc. The prodromal phase of progressive degeneration of the DA of neurons until symptoms appear, which proves the existence of compensatory mechanisms in the early stages of PD [9,10].

Visual function can be important in predicting dementia in PD. In a prospective study, abnormal color vision at baseline tripled the probability of developing dementia [11]. Some non-motor symptoms can be detected early in the disease, at which time affordable treatments can be initiated to prevent progression. Other non-motor symptoms are more resistant and require the introduction of new drugs. Visual impairments in PD can be caused by pathological mechanisms such as retinal dopamine depletion or reduced innervation to the visual cortex. [12]. Most visual impairments are curable or preventable, so early diagnosis is clearly crucial [13]. The presence of visual and visual impairments in PD patients remains grossly underestimated by neurologists and general practitioners. The preservation of the eye organ function is particularly important for patients with PD due to their need to compensate for locomotor automaticity disorders, including unstable postures [14]. Visually-spatial disorders, one of the life-threatening manifestations of the disease, have been insufficiently studied so far [15]. These include double vision, a change in contrast sensitivity and color vision, a feeling of sand in the eyes, as well as psychotic syndromes associated with visual impairment: illusions and hallucinations [16,17,18].

# The Objective

To study visual non-motor disorders in PD patients in Almaty for optimization of diagnosis and correlation with the duration and severity of disease.

#### **Materials and Methods**

This is a prospective study of ambulatory patients observed in various polyclinics of Almaty, which is the major city of Kazakhstan.

Symptoms were rated in a group of 106 patients with PD (64 women and 42 men) using the Movement Disorder-Unified Parkinson's Disease Rating Scale (MDS-UPDRS; alpha-Kronbach =0,979). A total of 61.9% of the subjects were Asian, and 38.4% were European; all of them were eligible. All patients were diagnosed with PD by the British Brain Bank.

The control group consisted of 54 neurologically healthy individuals of the relevant age and sex, from the database of polyclinics in Almaty, regardless of nationality. The total number of people studied, including the control group, was 160. Personal information was encoded by unique identifiers. All patients or their legal representatives have given informed written consent to participate in our study. Prior to the start of the study, all PD patients filled out a form for visual impairment in Parkinson's Visual impairment in Parkinson's Disease Questionnaire (VIPD-Q) (available in the public domain).

The questionnaire also assesses the effects of eye symptoms on everyday activities. Patients with significant concomitant and ocular pathology that may increase the unreliability of the results were excluded from the study.

The research paper defined the main demographic and clinical characteristics, including age at the time of the study, age and duration of the disease, Parkinson's history, Levodopa response, UPDRS score (unified Parkinson's scale) and the clinical subtype of PD. The severity of the disease and stage was estimated by the Hoehn & Yahr Scale (1967). Motor disability was evaluated with the help of the revised MDS-UPDRS, Parts II and III.

For the determination of cognitive function, the Montreal Cognitive Assessment (MoCA), the Non-Motor Symptoms Questionnaire (NMSQ; 2006), and the Hospital Anxiety Scale and Depression (HADS; 1983) were used; early and late visual symptoms were evaluated with the Popelreiter test and the Yerkes test; the Mirror letters and test numbers were used to determine visual and spatial impairments. Test with an assessment of the position of the hands on the clock), Rupp's Test, noise images, and Raven's Progressive Matrices were also used.

The questionnaires were filled in by the patients themselves or their relatives, or by a doctor when the patients did not fully understand the question or had pronounced motor disorders. Data processing was done using IBM SPSS Statistics version 27.0 for Windows and Datawrapper.

The highest number of patients was in the group over 60-80 years of age. The age of patients ranged

from 40 to 90 years; the average age of patients with PD was 69.72+0.732 (female-64, male-42) and

in the control group was 67.54+0.561 (female-38, male-16) (Figure 1).



Figure 1 - Pareto diagram comparing PD patients and controls according to age

The average duration of the PD was 15.04+0.74 years (women 14.52+0.6 years, men 16.24+0.4 years; no significant difference; p>0.05). The

average age at the time (onset of symptoms) of illness was 58.23+0.652 years (men  $61.25 \pm 1.45$  years, women  $56.13 \pm 2.57$  years). (Figure 2).



Figure 2 – Pareto diagram in comparison of PD patients by gender and age

# **Results and Discussion**

The majority of PD patients presented with the akinetic-rigid form of PD (55,6%; n=59)

patients), followed by the tremor dominant form (23,25%; n=25) and the mixed form (20,7%; n=22) (Table 1).

Table 1 – Demographics and Disease Characteristics

Parameters		PD patients		Controls	
Total number	of observed patients	(n =106)	%	(n =54)	%
male	· – –	42	37,7%	16	29.63%
female		64	62,26%	38	70,37%
Level of educ	ation		·		
Graduate		65	61,32%	32	59,26%
Undergraduat	te	10	9,43%	9	16,67%
Secondary		17	16,04%	8	14,81%
8 and less gra	ıdes	14	13,21%	5	9,26%
Average age a	at time of study	69,72±0,732		67,54±0,561	
Average age a	at the diagnosis,	58,23±0,652		-	-
female		56,13±2,57			
male		61,25±1,45			
Average dura	tion of illness, years	15,04±0,74		-	-
female		14,52±0,6 16,24±0,4			
male		0.00			
MDI duration	n PD (years)	от 0 до 29		-	-
The form of a	isease	25	22.50/	-	-
Iremor		25	23,5%	-	-
· Akinetic	-rigia	39	33,0%	-	-
Stage of disco	ass on Hoshn and Vahu se	22	20,7%	-	-
DD	Stage 1	10	0 1 %	-	-
ID	Stage 1 5	2	2 80/	-	-
	Stage 2	25	2,870	-	
	Stage 2 5	23	7 5%	-	-
Control	Stage 3		41 5%		
Control	Stage 4	14	13 2%		
	Stage 5	2	1 8%		
		2	1,070	-	
Parameters		PD natients		Controls	
Total number	of observed	(n = 106)	%	(n =54) %	
Male	0,0000,000	42	37.7%	16	29.63%
Female		64	62.26%	38	70 37%
Level of educ	ation		02,2070		10,2110
Graduate		65	61.32%	32	59.26%
Undergraduat	te	10	9.43%	9	16.67%
Secondary		17	16.04%	8	14.81%
8 and less grades		14	13.21%	5	9.26%
Average age at the moment of study		69,72±0,732	- ,	67.54±0,561	- ,
Average age a	at the moment of illness,			-	-
female		58,23±0,652			
male		56,13±2,57			
		61,25±1,45			

Average duration of illness, years				-	-
female		15,04±0,74			
male		14,52±0,6 16,24±0,4			
MDI duration	PD (years)	от 0 до 29		-	-
The form of d	isease			-	-
· Tremblin	g	25	23,5%	-	-
· Akinetic	-rigid	59	55,6%	-	-
• Mixed		22	20,7%	-	-
Stage of disea	se on Hoehn and Yahr s	cale		-	-
1 group	Stage 1	10	9,4 %	-	-
	Stage 1.5	3	2,8%	-	-
	Stage 2	25	23,6%	-	-
	Stage 2.5	8	7,5%	-	-
2 group	Stage 3	44	41,5%	-	-
	Stage 4	14	13,2%	-	-
	Stage 5	2	1,8%	-	-

Some authors note the importance of pathophysiological differences between motor symptoms, although both are usually associated with changes in the motor cortex and basal ganglia. According to literature, akinetic-rigid syndrome is more closely associated with the anatomical functional changes of the motor hinges of basal ganglia, especially in the projections of globus pallidus, with external and internal parts, thalamus and eventually the motor cortex [16]. In contrast, the symptoms of tremor (Dirkx, M. F. et al. 2016) are associated with pathological interactions between the globus pallidus and cerebellar pathways [17].

Many authors point out that motor akinetic-rigid syndrome correlates with a worse prognosis and an increased risk of dementia compared to the shaking subtype of PD [19]. Our results also show that the more severe cases were statistically more frequent (p<0.001) in the group with akinetic-rigid syndrome.

The severity of the disease in the patients we examined corresponded on the Hoehn and Yahr scale mainly to 1-2-3-4 stages; on average  $2.75 \pm 0.148$ .

(Figure 3).



Figure 3 – Box diagram of PD patients' distribution according to Hoehn µ Yahr scale on duration of disease

The results show that patients with mild or moderate two-way symptoms with 41.5% (44) already having visual and cognitive impairments are more prevalent among PD patients and they remain independent at home, but cannot overcome the retropulsive-pull test. Patients with bilateral manifestations without postural instability accounted for 23.6% (n=25). In third place, patients with severe disability, with a number of motor symptoms, could get up and walk unaided on «good» days or hours 13.2% (n=14) (Figure 4).



Figure 4 – Histogram of PD patients according to Schwab and England Activity scale in %.

A total of 51,89% (n=55) patients experienced a slow course of the disease, characterized by stage changes for 5 years or more; 33.96% (n=36) had a moderate progression rate, with stages changing over 2-5 years. About 14.15% (n=15) of patients had a rapid progression of the disease, with stages progressing over two years or less.

The majority of PD patients (87.74%; n=93) had visual impairments. Seventeen (18.28%) of them had symptoms in the early months and years prior to diagnosis of PD. Most frequently, patients complained of weak and fatigued eyes, dry eyes, vague (reading or working with a computer for a while), difficulty in reading, poor orientation at twilight or poor lighting (often encountered with objects or people), visual hallucinations, and color impairment (colors appear paler than before).

Screening of cognitive functions (using the MMSE scale) is important, allowing early detection of initial impairments and preventing or correcting significant declines in the quality of life of patients and caregivers. According to Aarsland et al. (2007), dementia affects on average up to 40% of patients; it

is likely that almost 80% of patients in the final stage of the disease will have dementia [20]. Cognitive decline among our patients was 61.32% (n=65) in the core group, taking into account the criteria for excluding patients with severe dementia from the Short-Term Mental Assessment (MMSE) study below 21. Clinical dementia in PD is characterized primarily as a syndrome of executive dysfunction, action planning, spatial-visual impairment and only later memory impairment.

Patients often complained of elementary and subject-specific hallucinations, a sense of the presence of an outsider in the apartment, photopsias and spots in their eyes. In some patients, visual hallucinations occurred while falling asleep or waking up. Three patients described movement hallucinations that developed in the early stages of the disease prior to the initiation of Parkinson's therapy. Our study found that visual hallucinations were more often combined with cognitive deficits, and longer-term illness. The most difficult patients to treat were long-term patients with both PD and visual hallucinations. Most (81.25%) visual hallucinations in patients with PD were combined with cognitive deficits, with duration of over 20 years. Of these, 37 patients had pre-dementia cognitive impairments with MMSE scores ranging from 22 to 27; 28 patients had mild dementia scores of 20-23 on the MMSE scale (Figure 5).



Figure 5 – Tables of concordance of visual hallucinations in PD patients according to the MMSE (brief mental status assessment scale)

We have analyzed correlations between visual impairment parameters and MMSE, MoCA, anxiety,

cognitive test, PD group watch test and control group (Table 2).

	MMSE	MOCa	anxiety scale	cognitive	clock
				test	test
dry eye	-,508**	-,508**	-,535**	-,542**	-,617**
weakness and eye fatigue	-,397**	-,397**	-,464**	-,438**	-,543**
blurred vision (do you have blurred vision, for	-,462**	-,462**	-,484**	-,508**	-,543**
example, when reading or working with a computer					
for a while?)					
	1.50**	1.5.0 **	- 4 4**	<b>50</b> 0**	500**
difficulty reading	-,452	-,452	-,544	-,528	-,528
poor orientation at dusk or in low light (do you	-,476**	-,476**	-,497**	-,536**	-,557**
bump into objects or people?)					
visual hallucinations	-,386**	-,386**	-,401**	-,421**	-,487**
color vision impairment (colors seem paler than	-,415**	-,415**	-,522**	-,471**	-,523**
before?)					

Table 2 – Pearson correlation of visual impairment and MMSE, MoCA, NMSQ, anxiety, cognitive test, and clock test scales(n=159)

We found statistically significant correlations between visual impairment and cognitive function in both MMSE and MoCA, as well as anxiety test scores (p<0.01); visual hallucinations were not statistically significant across all cognitive parameters. Note that dry eye was significantly correlated with almost all parameters: MMSE and MoCA (-,508\*), anxiety (-,535\*), cognitive test (-,542\*\*), and clock test (-,617\*\*). The extent of cognitive disorders in PD patients ranged from lack of cognitive impairment to mild dementia according to the MMSE scale and is also one of the three main predictors of PD and dementia risk. Both groups were tested using the NMSQ questionnaire. Most PD patients are diagnosed with one or more NMS during their illness.

The average number NMS per patient with PD was 10 as compared to 4 in the control group (p< 0.001). The total number of NMS in PD ranged from 1 to 28, with the highest incidence of 10 or more symptoms per patient in 66.98% (n=71) patients and less than 10 NMS in 33.02% (n=35) of patients (Figure 6.)



Figure 6 – Results of the non-motor symptom questionnaire (NMSQ) in the group of patients with PD and visual disorders.

The following symptoms were significantly more frequent in the PD group than the control group: hypersalivation, hyposmia, dysphagia, difficulty in concentrating and maintaining attention, intense and vivid or frightening dreams, anxiety, fear, panic, nausea, vomiting, constipation, and increased sweating (all p<0.001). NMSs often occurred early in the disease, and in 11.32% (n=12) patients pre-motor, doctors did not pay sufficient attention to these symptoms, so there was no proper correction. In the later stages of PD, non-motor manifestations begin to dominate as factors which affect the patient's quality of life and become more important and disabling at certain moments by motor fluctuations, causing insurmountable difficulties for the patients and their caregivers. The diagnosis of PD was based on the detection and identification of specific motor manifestations that are direct consequence dopaminergic of insufficient transmission in the nigrostriatal system. The set of nonmotor symptoms we have identified from the NMSQ questionnaire turns out to be equally characteristic of the disease, most of which are non-dopaminergic in nature.

According to the literature, visual impairments are common in PD, but their exact frequency and severity are unknown. Good visual function is crucial for patients with PD as they need to compensate the loss of automatic motor control and unstable posture, forcing patients to direct their movements visually [21]. Awareness and early recognition of eye and visual problems in PD can lead to timely individualized treatments leading to safer patients, greater independence and better quality of life. Nonmotor visual impairments in PD can be detected early [22]. Figure 7 shows visual impairments depending on the duration of the disease in descending order: dry eyes, color impairments and visual hallucinations, etc.

# Conclusion

The early detection of visual non-motor symptoms greatly expands our understanding of the disease by demonstrating its complex nature, which goes far beyond conventional knowledge. When planning therapeutic strategies for PD in clinical practice, doctors tend to focus primarily on motor symptoms, and non-motor symptoms are often



Created with Datawrapper

Figure 7 – Bar chart with the accumulation of visual impairment as a function of the duration of PD (Datawrapper)

unrecognized and underestimated. Special measures to improve visual non-motor disorders will lead to increased patient safety, greater autonomy, better quality of life and better medical care. Vision problems may precede the onset of the disease itself and may serve as an early marker for PD.

In our study, 18.28% (n=17) of cases had visual problems in the early period. Moreover, vision

problems can also help predict the progression of cognitive impairment, dementia, and PD itself. Currently, we are actively searching for biomarkers of PD and cerebrovascular diseases capable of predicting the development of the disease, determining the rate of progression of the disease, evaluating the effectiveness of the therapy conducted at the molecular level [23,24,25].

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# FREQUENCY OF ATONIC UTERUS DUE TO PRIMARY POSTPARTUM HEMORRHAGE: A CROSS-SECTIONAL STUDY

Postpartum hemorrhage (PPH) is loss of 500mL of blood from genital tract after normal vaginal delivery or 1000mL after cesarean section. PPH is one of an important cause of maternal mortality and morbidity worldwide, the only strategy that has shown a significant reduction in maternal mortality in patients with PPH is active treatment and management of third stage of labor.

In this study we aim to determine the frequency of atonic uterus due to postpartum hemorrhage.

A descriptive cross-sectional study was carried out on women attending at Shar –Ara teaching hospital in Kabul from 1<sup>th</sup> January 2020 -1<sup>th</sup> January 2021.

In general, this study included 170 women with postpartum hemorrhage out of these 105 (61.8%) of whom had uterine atony, followed by other causes retained placenta tissue 22.4%, genital tract tears 14.7%, coagulopathies at 1.2%. It was found that 53.3% of patients were between 20-28 years old, 43.8% women were grand multipara, 87,6% cases were seen in full term pregnancies while 9.5% in post term pregnancies. 92.4% of women were found with previous history of PPH. Finally 47.6% cases managed by uterotonic agents (Metergin + Misoprostol + Oxytocin), 13.3% – only by Misoprostol, 10.5% – by Oxytocin + Misoprostol are used. B lynch compression sutures and uterine courage and massage was performed in 9,5% cases while 1.9% total abdominal hysterectomy was performed.

In our study the frequency of uterine atony due to postpartum hemorrhage was found in 61.8% of cases. Most cases have been seen in women with full term gestational age, and Uterine atony is common in grand multipara, and young patients. Uterine atony mostly managed by uterotonic agents. Any delay in diagnosis and managements of PPH lead to maternal death and disability.

Key words: Postpartum Hemorrhage, Uterine Atony, uterotonic agents, compression sutures

# Introduction

Postpartum hemorrhage (PPH) is defined as the loss of 500 mL of blood from the genital tract following a normal vaginal delivery or 1,000 mL after a cesarean surgery. PPH is one of the leading causes of maternal mortality and morbidity worldwide. Obstetric hemorrhage is thought to be responsible for around a quarter of all maternal deaths, and nearly half of all postpartum deaths [1]. In high income countries the absolute risk of death from PPH is substantially lower, with an estimated of 1:100 000 deliveries compared to 1:1000 in low-income countries [2].

The prevalence of maternal deaths due to obstetric hemorrhage, the single most common cause of maternal mortality and morbidity, varies substantially, according to a recent WHO analysis of maternal deaths in high income countries, hemorrhage is responsible for 13,4% of maternal mortality, whereas in Africa and Asia, it is responsible for 34 and 30,8% respectively [1, 3].

The most dangerous consequence of third stage of labor is an atonic uterus, the uterus fails to retract resulting in severe bleeding. Attributable to quick or protracted labor, the failure of contraction and retraction may be due to intrinsic myometrial dysfunction. Primiparas and grand multiparas are more prone toit [4, 5, 6]. The most prevalent cause of PPH is uterine atony (65%), genital tract trauma (33%), retained placenta (27%), coagulation abnormalities and uterine rupture [7, 8, 9, 10].

Previous history of PPH, grand multiparity, injudicious use of oxytocin, extended labor, birth of a baby weighing more than 3.5 kg, home delivery and instrumental delivery are all major risk factors for atony [4, 10, 11].

Afghanistan is one of the countries in the world with the highest maternal mortality rate, and the deaths of mothers and children are a top priority for health programs and the international community. Health interventions to prevent maternal mortality due to PPH are emerging in developing countries.

PPH not only causes a slew of issues for the mother but it also affects her financially, socially and psychologically as well as her family. All of this could lead to family and societal disintegration.

The purpose of this study was to identify the facts about PPH caused by uterine atony. The findings of this study are being used to develop methods to reduce of maternal mortality. However, we feel that using a diverse set of data sources enabled us to develop through suggestions for further research and management of this condition.

# Materials and research methods

A descriptive cross-sectional study was carried out on women attending at Shar –Ara teaching hospital in Kabul from 1th January 2020 – 1th January 2021. We employed convenience sampling during this period on 170 patients with primary PPH. The study was carried out in the Department of Obstetrics and Gynecology. The study population included all cases admitted with primary PPH during the study period. For calculation of frequencies, the total number of deliveries in the setting during the study period was used.

A comprehensive obstetrical clinical workup was performed on all participants, which included a histor, general physical examination, abdominal and pelvic examination and relevant laboratory investigations. The maternal condition was assessed and managed according to established hospital protocols which included both pharmacological and surgical intervention out of 105 of these, all patients with uterine atony included in this study.

Essential information about the cause of PPH, age, gravidity, gestational age, previous PPH history and management of uterine atony were gathered from patient profiles who were diagnosed and managed for PPH in case of uterine atony after extensive review during this period from delivery room (emergency department), operation room, medical records and the electronic database. Women delivered inside the hospital and occurred PPH due to uterine atony in first 24 hours, women whose delivered vaginally and followed by PPH (atony) included in the study. However, patients who have delivery by cesarean section and followed by PPH, women who had PPH by other causes, secondary postpartum hemorrhages were excluded. The data was entered and analyzed using SPSS 2.0. Frequencies and percentages were calculated for variables.

# Results

Total number of deliveries during the period of study were 950 cases. Total number of patients with PPH was 170 that the frequency of PPH in first 24 hours was 18% (figure 1).



Figure 1 – Frequence of postpartum hemorrages

The leading cause of primary PPH was uterine atony 61.8% (105 out of 170), followed by other causes retained placenta tissue 22.4%, genital tract lacerations and tears 14.7%, coagulopathies at 1.2% (table 1).

Table 1 – Most common cause	of postpartum hemorrhage	
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Causes of PPH	Number	Percent
Uterine Atony	105	61,8
Retention of Placenta tissue	38	22,4
genital tract lacerations and tears	25	14,7
Coagulopathy	2	1,2
total	170	100

We found that most cases (53.3%) the maternal age of women with uterine atony were between 20-

28 years old and minimum cases were seen in women aged more then 45 years old (table 2).

Table 2 – Age distribution among women with uterine atony

years	Number	Percent
<19	30	28,57
20-28	56	53,33
29-36	16	15,24
37-45	1	0,95
>45	2	1,9
total	105	100

The number of parity of women with uterine atony is presented in table 3. I was found that 43.8% women were grand multipare (5-7), 26,7% women had 2-4 pregnancy.

Table 3 – Number of parity of women with uterine atony

Parity	Number	Percent
1	20	19,0
2-4	28	26,7
5-7	46	43,8
>8	11	10,5
total	105	100

It was found that 87,6% of women with uterine atony were seen in full term pregnancies, 9,5% – post perm and 2,9% – pre term pregnancies (table 4).

Gestational age	Number	Percent
Full term (37–41)	92	87,6
Post term (>41)	10	9,5
Pre term (<37)	3	2,9
total	105	100

Women with uterine atony had previous history of PPH in 92,4% of cases and in 7,6% – had

not previous history (table 5).

Table	5 –	Previous	history	of PPH	of women	with	uterine ato	ny
								~

Gestational age	Number	Percent
Non-existed	8	7,6
existed	97	92,4
total	105	100

The table 6 shows medical treatments and procedures are used for managements of uterine atony and most cases managed by uterotonics agents (79%).

Women with uterine atony were managed by uterotonic agents with three agents (Metergin + misoprostol + oxytocin) in 47.6% cases, 13.3% –

only by Misoprostol, 10.5% – by Oxytocin+Misoprostol, 7,6% – by Metergin + Misoprostol.

Uterine courage and massage were performed in 10 patients (9,5%), B-lynch compression sutures were applied in 10 patients and in 2 (1,9%) – hysterectomy (table 6).

	Number	Percent
uterotonic agents (Metergin + misoprostol + oxytocin)	50	47,6
Only Misoprostol	14	13,3
Misoprostol + Oxytocin	11	10,5
Metergin + misoprostol	8	7,6
B lynch	10	9,5
uterine courage and massage	10	9,5
hysterectomy	2	1,9
total	105	100

**Table 6** – Management of uterine atony

#### Discussion

In the third stage of labor and delivery, as well as in the postpartum period, PPH is a significant and common complication, in our study, where 170 cases of primary PPH were found (18%).

The incidence of primary PPH was 9.6% in a research by Ara belgees [4], which is within the expected range of 5 to 8% described in the global literature according to Sabrina et al. findings [11].

The study, conducted by Ashraf T in Quetta, Pakistan, on 13,850 deliveries between January 1993 to December 1996, reported a PPH frequency of 2.4% [12], which is quite low when compared to global data, the causes for the low incidence were not indicated in the previous study; however, the length of the study, the characteristics of population, referral biases and natural inclinations may have all contributed to the wide range of frequency estimates, studies by Prêtvill and Adetor have shown a PPH rate of 10-20% [13, 14].

The frequency of PPH (20.9 %) was reported by Drissen M Sever, and the results of these studies are quite similar to our findings [15].

According to our findings uterine atony is the most common cause of PPH, accounting for 61.8% cases. Other causes of PPH include retention of placenta tissue (22.4 %), genital tract injuries or tears (14.7%) and coagulopathies (1.2%). Uterine atony was the most common cause of primary PPH in the study by Ara B (57.6%), followed by retained placenta tissue (21.6%) and genital tract injuries (18.7%) [4]. Driessen M results reported approximately 75% of PPH are followed to uterine atony [15], also Homira Naz study revealed the most common cause of primary PPH was uterine atony, which was found to be 58% of cases [16]. Uterine atony was also identified as the most common cause of PPH in a study conducted in Rawalpindi, Pakistan, with 65% of cases having this condition [12].

According to Sabrina and Japaraj's international reports uterine atony was the most common cause of PPH, accounting for 50% to 76% of cases [11, 17]. In result of H Nazi the second most common cause of primary PPH was vaginal, cervical and perineal tears (24%) [16].

Sabrina and Rizvi F's studies also found a higher prevalence of traumatic lesions as a cause of PPH, ranging from 9% to 20% of cases, fol-

lowed by tears (34.7%). The frequency of retained placenta were (17.3%) of cases [11, 18]. Retained placenta reported in 6% of Cases by Nazi [16]. According to a study by Shaheen from Pakistan, the retained placenta occurs in 27 % of cases [9]. In comparison to our findings, a study by Ashraf T, indicated that the frequency of retained placenta was determined to be 37% [12], this difference simply indicates that we did not have any refer cases because all of the cases were delivered in hospitals, whereas the population under study in other studies was from patients who wanted to deliver in hospitals or refer cases due to PPH from private clinics, and there were no cases of retained placenta in hospital deliveries. In 1% of cases coagulation cascade disorders and platelet dysfunction are the cause of postpartum hemorrhage [19], this conclusion is identical to our finding.

Patient demographic profiles with PPH also gave useful information, our findings revealed that 53.3% of women were between the ages of 20-28 years old, in comparison to international figures, the age profile of the subjects was lower, according to study by H Nazi, the age of patients was 34% between 21-25 years old, but Sabrina state the majority of cases are above 35 years old, and the majority of patients, in the H Nazi investigation (82%) were under the age of 35 years [16].

The explanation for this disparity may be due to the younger age of marriage in general, which is connected with increased gravidity and parity at younger ages, however, the majority of the patients in Ara B study (65%) were between the age of 21-30 years [4], this is similar to the Adetoro study, in which the majority of the patients were between the ages of 20-28 years, all of these studies are very similar, the age of the mother did not appear to be related to the presence of an atonic uterus[14].

Grand multiparity was found to be a major risk factor for atony in our study, with the majority of women 54.27% being grand multipare (having more than 4 children) and 20% being primigravide while out of these (43.6%) had 5-7 children. In a study by H Nazi, the number of multiparous females were 82%, whereas primigravida was only 18%, as a result, the current study suggests that multiparity is a risk factor for PPH [16].

In our results (87.6%) cases were found in full term pregnancies while 9.5% in post term pregnancies. In study by Driessen M the majority of atonic uterus (78.5%) cases were found in full term pregnancy (37-41 weeks), 4.8% in preterm, while 16.7% in post term pregnancy (>41weeks) [15].

Montufar-Rueda C, mean of gestational age with atonic uterus was found  $(37.6 \pm 3.2)$ . The outcome of these studies revealed that preterm and postterm pregnancy are not important for atonic uterus [20].

According to our findings, 92.4% of women with atonic uterus had previous history of PPH, while 7.6% of women had not a history of PPH.

According to Oberg AS findings, women with a history of PPH have a threefold greater risk of PPH in subsequent pregnancies [21]. In a study by Ara B, 46.3% of women with a past history of PPH were found to have an atonic uterus during their current delivery [4], while a study by Driessen M found that 20.9% of women with atonic uterus had a previous history of PPH [15]. These studies differ from our finding because these studies looked at all probable causes of PPH, whereas we only looked at uterine atonia and vaginal delivery. In our study, uterotonic drugs (Metergine+Misoprostol+Oxytocin) were used in 47.6% of cases, misoprostol was used in 13.3% of cases, and oxytocin +Misoprostol was used in 10.4% of instance, 9.5% B lynch and 9.5% uterine courage and massage were conducted, whereas 1.9% total abdominal hysterectomy was performed. Approximately most cases managed by uterotonics agents (syntometrine, oxytocine) and uterine massage were found to decrease bleeding in 53.7% of cases in a study by Ara B and Prostaglandins were shown to be effective in 68.7% of cases, uterine packing was performed in (62.5%), in 7.5% of instances, uterine artery ligation was effective (80%) [4].

According to a study by H Nazi, pharmacological management was used in 94% of cases, followed by surgical management in PPH cases. The current study likely to a free with such findings [16]. Disparities in measurements and time variations, access to health facility, resources, family barrier, capacity of health staffs, ANC of pregnant women concern could all contribute to variance and however, some of the findings of studies are similar to our results.

# Conclusion

In our study the frequency of uterine atony due to postpartum hemorrhage was found in 61.7% of cases. Most cases have been seen in women with full term gestational age, and Uterine atony is common in grand multipara, and young patients. Uterine atony mostly managed by uterotonic agents. Any delay in diagnosis and managements of PPH lead to maternal death and disability.

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# EXPERIENCE IN USING INTRAUTERINE BALLOON IN EARLY POSTPARTUM HEMORRHAGE

Early postpartum hemorrhage holds a position within the top reasons of maternal mortality, in spite of the fact that it is one of the manageable reasons. The risk of postpartum hemorrhage is worsened by Coronavirus pandemic due to dysregulation of hemostatic system in this disease. The use of intrauterine balloon gives an opportunity to affect the uterine tonus and mechanically close lumen of vessels gaping during postpartum hemorrhage. The world research medical books represent several works devoted to the use of intrauterine balloons and every researcher highlights its high efficiency, ease of use and minimal amount of side effects. In our research work we used 6 balloons in early postpartum hemorrhage and achieved affects in 83.3%. In 16.7% we had to do hysterectomy, in 16.7% we had to perform surgery to stop the hemorrhage, i.e. to do B-Lynch compression suture. The presence of balloon in uterus did not lead to any suppurative-septic complications, nor changed the parameters of coagulation test and biochemical blood test. The Hb level remained stable both when balloon was in the uterus and when discharged from hospital. Thus, the use of balloon to stop early postpartum hemorrhage has proven its efficacy confirmed during practical experience and evidence-based sources.

Key words: early postpartum hemorrhage, intrauterine balloon, uterine tonus, hysterectomy, B-Lynch compression suture.

#### Introduction

Early postpartum hemorrhages rank as one of the top reasons of maternal mortality in the world. The National Vital Statistics System (NVSS) reports that in 2018 the maternal mortality rate was 17.4, in 2019 this rate became 20.1 per 100 thousand of live births, [1], in 2020 we failed to find any accurate information in the open sources on maternal mortality rate. «In Kazakhstan maternal mortality rate has increased 20.8 times, states the President Kassym-Zhomart Tokayev during the extended session of the Government. As per the report of the Minister of Health, «The maternal mortality rate in 2020 reached its tragic thresholds, since it increased almost three times and made up 36.5 per 100,000 live births against the planned value of 17.1. In addition 36.5 is an average level for the Republic. As for the other regions the numbers are more frightening and reach up to 70, sometimes up to 95 per 100,000 live births» [2]. According to the Lancet, the reasons of maternal deaths in 2014-2019 comprise early postpartum hemorrhages, then hypertensive

complications [3], and the reasons of deaths have not changed. In COVID-19 environment the number of postpartum hemorrhages increased mainly due to pathogenesis of injury of blood coagulation system by the virus [4].

When arresting massive postpartum hemorrhage there is a large role of impact on all the factors that lead to hemorrhage arrest, i.e. on blood coagulation system, uterine tonus and vessel lumen. Insertion of intrauterine balloon has an impact both on uterine tonus and vessel lumen. The method of inserting intrauterine balloon [5,6,7,8,9,10] is used throughout the entire world and is presented in the clinical practice guideline of the Republican Center for Health Development «Postpartum Hemorrhage» as of 2016 [15].

We have conducted an effectiveness study of intrauterine balloons produced by a local company «Almerek» to treat early postpartum hemorrhage.

### **Materials and Methods of Studies**

Intrauterine balloons were randomly inserted to 6 women who had postpartum hemorrhage.

Study methods included clinical and statistical ones. Intrauterine balloon consists of silicone balloon, two hollow pipes, two syringes and two caps. A fluid injected into the balloon creates required pressure in the cavity of uterus. The techniques of balloon tamponade are as follows. In case of 500-600 ml blood loss and unstable uterine tonus revealed upon manual examination the balloon was inserted into the uterus cavity and the top of the balloon folded dome reached the uterine fundus. Further saline solution was injected to the balloon with two syringes by turns. Usually in 10-15 minutes, rarely in 60 minutes there appeared signs of restoring contractile function of uterus. No bleeding in the pipe located in the vagina within 30-40 minutes allowed considering that tamponade was

complete and successful. Similar techniques were performed with 6 obstetric patients. The balloon is equipped with two syringes for quick intake of required volume. The syringes were fixed and later could regulate volume in the balloon. There is also a special drainage to control possible bleeding. The patients did not have any sense of discomfort and stayed in the post-natal wards with the balloon located in their uterus cavity under the supervision of paramedics.

The age of women varied between 25 and 41, whereas the average age was  $32.3\pm0.6$ . The parity comprised 1 to 6, average parity being 3.3. Among them 3 were pulripara (50%), 1 with burdened anamnesis (16.7%). Figure 1. shows gestation course and complications with patients.





Thus, patients during the gestation period frequently demonstrated moderate anaemia 66.7%, 1 patient was with asymptomatic bacteriuria (16.7%),

1 with low placentation and 1 with STD in our case it was ureaplasmosis. Diagram 2 shows extragenital diseases of patients.



The top extragenital diseases include anaemia (50%), and 1 case (16.7%) in each of chronic arterial hypertension and thyroid disorders.

All patients performed delivery naturally fullterm, of which 2 (33.3%) had labor induction because of gestational arterial hypertension (16/7%)and tendency to postterm pregnancy (16/7%). Length of labor did not exceed physiological values and constituted 5 to 9 hours. Duration of the second period of labor took 20 to 65 minutes. All children were born in good condition with Apgar score being 7-8. Fetal weight varied between 2,885 and 4,865 g, average fetal weight was 3806±200. One patient (16.7%) had a bleeding in 15 minutes after delivery, the rest had it in 5 minutes after delivery. Catheter insertion took about 3 to 5 minutes and in 20-50 minutes (on the average 28 minutes) hemorrhage was arrested. Duration of balloon presence in uterus lasted from 4 to 7 hours, on the average being 5.4 hours. One patient (16.7%) had hemorrhage continued which led to hysterectomy, total blood loss was 2,000 ml. In addition another patient had to have B-Lynch compression sutures, but the reproductive function was preserved. Maximal Hb level decrease (76g/l) was observed with one patient (16.7%)who had hysterectomy. She also had her coagulation test results changed to hypercoagulation and slight hypoproteinemia and hyperglycemia. For the remaining women parameters of blood coagulation and biochemical indices remained stable. Hb level of women being discharged varied between 87 and 111 g/l, on the average being 103.17g/l. Total extent of blood loss was 700-2,000 ml, on the average - 941.67±220 ml. Clinical blood analysis of 2 women (33.3%) being discharged from hospital showed slight leukocytosis, whereas it was within the normal limits with the rest. Duration of staying in maternity clinic varied between 2 to 6 days, on the average -3.33 days.

Table 1 – Patients' Data	
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N	Age, years	EGD and gestation course	Parity	Delivered course	Extent of blood loss, ml	Fetal weight, g	Duration of balloon being in uterus	Hb g/l	Outcome
1	41	Anaemia, STD	P-5, C-5	1 <sup>st</sup> period – 5 hours, 2 <sup>nd</sup> period 40 minutes	800	4280	6 hours	106	Discharged
2	35	Anaemia, autoimmune thyroiditis	P-6, C-5, A-1	1 <sup>st</sup> period 4 hours 40 minutes, 2 <sup>nd</sup> period – 20 minutes	800	4100	7 hours	107	Discharged
3	35	Anaemia,	P-2, C-2	1 <sup>st</sup> period – 9 hours 30 minutes, 2 <sup>nd</sup> period – 35 minutes	850	3478	6 hours	107	Discharged
4	32	Asymptomatic bacteriuria	P-4, C-4	1 <sup>st</sup> period -9 hours 15 minutes, 2 <sup>nd</sup> period – 21 minutes	800	4865	4 hours	111	Discharged
5	25	Anaemia, low placentation	P-1, C-1	1 <sup>st</sup> period – 9 hours 15 minutes, 2 <sup>nd</sup> period – 65 minutes	900	220	4 hours	101	B-Lynch seams
6	26	Anaemia, gestational hypertension, affected by chronic arterial hypertension	P-2, C-2	1 <sup>st</sup> period – 9 hours, 2 <sup>nd</sup> period – 22 minutes	2000	2885	10 minutes	76	hysterectomy

Given the small number of cases using the balloons, we have entered all data into table 1 for better analysis.

## Discussion

Early postpartum hemorrhage holds a position within the top reasons of maternal mortality, in spite of the fact that it is one of the manageable reasons. Thus, extending methodology of controlling bleeding is relevant to the whole world. In the world research books there are not many articles on how to use balloons, however, all sources somehow confirm their efficiency and ease of use. Some authors show efficiency of use being up to 99% [11,12,13,14]. The use of intrauterine balloons to arrest postpartum hemorrhage has efficiency of 66.6%, since in 16.7% only a hysterectomy had to be done, in 16.7% surgery had to be performed to arrest bleeding, i.e. B-Lynch compression suture. The presence of balloon in uterus did not lead to any suppurative-septic complications, nor changed the parameters of coagulation test and biochemical blood test. The Hb level did not critically decrease both when balloon was in the uterus and when discharged from hospital. We did not aim at calculating the economic efficiency of balloon, but it seems obvious now. Thus, the use of balloon to stop early postpartum hemorrhage has proven its efficacy confirmed during practical experience and evidence-based sources. Convenience of using locally produced balloons entails that this model has special appliances for syringes which allows quicker intake of required volume to fill the uterus cavity, and this is not provided in many of the foreign models.

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# URINARY TRACT INFECTION IN PATIENTS WITH BENIGN PROSTATIC HYPERPLASIA ADMITTED FOR PROSTATECTOMY

Urinary Tract Infection (UTI) in patients with Benign Prostatic Hyperplasia (BPH) causes UTI related complication before and after prostatectomy, reduction in their health-related quality of life and overall well-being, thus the knowledge of UTI may play a complementary role in management. The aim of this research was to study the prevalence of urinary tract infection (UTI), its causative organism and antibiotic susceptibility.

All BPH patients who were admitted for prostatectomy were included to the study. Information on age, presence of an indwelling catheter, other factors related to UTI and antibiotic susceptibility results were obtained and analyzed using IBM SPSS version 26.

Three hundred twenty six patients were studied. The age range of study participants was 51 to 89 years and displayed a median of 70 year (IQR=12). More than half of study participants 168 (51.5%) were between 61 to 70 years. Bacterial isolates were noted in 96 (29.4%) patients. Escherichia Coli noted in (25.3%) specimens was the most common organism isolated. The bacterial isolates were most-ly sensitive to imipenem, meropenem, and fosfomycin, but showed greater resistance to cefotaxime, ceftazideme and cefazulin accordingly. The age of study participants was significantly greater for those who had bacteriuria (Mdn = 70) years than those who did not have bacteriuria (Mdn = 67), U = 9569, P = 0.048. The same it was significant for PSA level (P = 0.000) but were not significant for prostate size (P = 0.558).

Less than one third of BPH patients had UTI (29.4%), E. Coli was the most common microbial cause of UTI in study participants it was the cause in one fourth of cases (25%), Imipenem group of antibiotic was the most sensitive antibiotics in study participants (93.9%), Cefotaxime was the most resistant antibiotics (66.7%)

Key words: Urinary Tract infection, benign prostatic hyperplasia, bacteriuria.

# Introduction

UTI is a bacterial invasion-induced inflammatory response of the urothelium that is normally accompanied by bacteriuria and Pyuria [1], or the presence of bacteria in the urinary tract is referred to as urinary tract infection [2]. Upper UTIs (pyelonephritis) and lower UTIs (cystitis, prostatitis) are categorized according to the site of infection, and uncomplicated and complicated UTIs are classified according to underlying conditions and structural or functional disorders of the urinary tract [3].

Urinary tract infection (UTI) is one of the most common infections in both outpatient and inpatient settings around the world, with 150 million people affected each year [4], every year, more than 8 million people visit a doctor's office in the United States [5]. The Centers for Disease Control and Prevention (CDC) estimates that UTIs cause 13,000 deaths per year, despite the fact that most patients only experience a variety of painful and irritating symptoms [6]. There are three components that make up a UTI. First, the patient must have clinical symptoms that point to a urinary tract infection. Dysuria alone or with fever, suprapubic discomfort, gross hematuria, costovertebral angle tenderness, or new or worsening urgency or urinary incontinence are all recognized clinical criteria in older adults [7].

Despite the fact that bladder outlet obstruction can affect both men and women, it is more common in older men. When the opening between the bladder and the urethra is partly or fully blocked, it happens at the base of the bladder. As a result, the disorder slows or prevents the bladder from emptying urine [8]. The most popular predisposing pathologies for urinary tract infection in adults with bladder outlet obstruction are benign prostatic hyperplasia and prostate cancer [9] BPH is characterized by hyperplasia of the prostatic stromal and epithelial cells, which results in the development of large, fairly distinct nodules in the periurethral region, which can cause partial or nearly complete obstruction of the urethra when large enough [10], Frequency, urgency, nocturia, trouble initiating urination, a sense of incomplete bladder emptying, reduced stream force, and stream interruption are all symptoms associated with BPH [11]. The causes of BOO differ between men and women. Noncancerous enlargement of the prostate, also known as benign prostatic hyperplasia, is the most common cause in men (affecting up to 70% of men over the age of 70) [12]

Urinary retention caused by benign prostatic hyperplasia (BPH) puts men at risk for urinary tract infection [13]. The addition of this complication to patients with obstructing prostates not only worsens their already poor health-related quality of life and social well-being, but also causes post-operative morbidity and puts a strain on health-care finances [14].

Urinary tract infection was seen in 35.9% and 34.6 percent of patients with benign prostatic hyperplasia and prostate cancer, respectively. The most popular microbiological agent isolated was Escherichia coli, and Nitrofurantoin, which has a high sensitivity to the pathogens, should be considered in the empirical treatment of the infection. The only independent indicator of infection was the existence of an indwelling urethral catheter. As a result, preventative measures for catheter-associated infections in these patients should be implemented [15].

Outpatient urine culture epidemiology provides valuable insight into the evolving prevalence and antibiotic susceptibilities of various uropathogens. Escherichia coli, which causes nearly two-thirds of cases in patients over 65 years old with uncomplicated cystitis, is the most common pathogen, followed by Klebsiella oxytoca (15% of cases), and Proteus mirabilis (15% of cases) (7% of cases). Gram-negative bacteria are found in more than 90% of cases of cystitis in older adults when taken together. 4 Catheter-associated UTI (CAUTI) has a more diverse microbiology [2].

In order to avoid septicemia and recurrent UTI, successful antibiotic therapy as well as adequate Urological intervention to eliminate predisposing factors and restore as much as possible the normal anatomy and function of the urinary tract are needed for the treatment of UTI in the presence of urinary tract obstruction [16].

In order to determine the most effective empirical antibiotic treatment for these patients, it is critical to have a good understanding of the possible species and local resistance trends. The rising prevalence of health-care-associated infections and the emergence of antibiotic resistance illustrate the importance of obtaining a definitive diagnosis, treating with effective antibiotics, and avoiding broad-spectrum antibiotics. Antibiotic resistance is on the rise, and it's starting to have an impact on the effectiveness of empirical antimicrobial therapy for urinary tract infections. The use of effective narrow-spectrum antibiotics depends on a correct diagnosis of urinary infections [17].

In Kazakhstan when choosing antimicrobial therapy, the Protocols for diagnosis and treatment recommend a microbiological study to determine antibacterial drug sensitivity, which was not done in 100% of cases, and initial treatment was empirically prescribed, with drugs from the cephalosporin group (Ceftriaxone) in 34%, nitrofurans (Furazidin) in 42% and flouroquinolones (Levofloxacine) in 24% of cases. In the majority of cases, alternative drugs were prescribed to treat acute cystitis, despite the fact that first-line treatment currently involves fosfomycin trometamol, pivmecillins, and nitrofurantoin macrocrystals, which according to the findings of this study were not used at all. Alternative antibacterial medications were prescribed in the majority of cases (71%) for the initial treatment of urinary tract infections. The majority of antibacterial medication dose regimens, dosage frequency, and treatment course did not follow current guidelines [18].

# Methodology

The study, retrospective and descriptive cross sectional in nature, was done at the urology department Scientific Center of Urology over a 2 years period (January 2019 – December 2020). BPH patients who were referred to the urology department and admitted for prostatectomy formed the study population. Three hundred twenty six patients who met the inclusion criteria within the period were studied.

# **Inclusion criteria**

All BPH patients in whom operation is indicated and admitted for prostatectomy.

# **Exclusion criteria**

Patients with prostate cancer

Patients with urethral stricture

Patients with urinary bladder neck sclerosis

Patients in whom conservative treatment was considered

Following informed consent of the hospital official for using the database of patients, a da-

ta collection form was designed and developed for each patient to record demographic characteristics, symptoms, and urine microbiology outcome. The size of the prostate on abdominal ultrasonography, as well as the prostate-specific antigen value, was recorded for all patients. Postvoid residual urine volume was recorded only in patients without acute retention of urine. Data were inserted and cleaned in Microsoft Excel 2010, then imported for statistical analysis in IBM SPSS version 26 data analysis package. Descriptive analysis, qui square test, logistic regression and for comparison of median of continuous variables a Mann Whitney U test were done the results presented in the form of tables, frequencies, and percentages. P < 0.05 was considered significant.

# Results

Three hundred twenty six patients with BPH who are admitted for prostatectomy during two years of 2019 and 2020 were studied, 194 (59.5%) of participants were admitted in 2019 and 132 (40.5%) were admitted in 2020, The age range of study participants was 51 to 89 years and displayed a median of 70 year (IQR=12). The PSA range of study participants was 0.002w5 to 100 nanogram/milliliter and displayed a Mdn PSA level of 6.185 ng/ml (IQR = 9.221), The range of postvoid residual urine of the study participants was 0 to 1737 milliliter and displayed a Mdn postvoid residual urine of 35 ml (IQR = 80), the prostate size range of study participants was 24 to 250 grams and displayed Mdn of prostate size of 63.5 gr (IQR = 29) (Table 1).

Table 1 – Median and IQR of age, PSA, PVRU and prostate size of Patients with BPH 2019 – 2020 (N=326)

variables	Median	IQR	Minimum	Maximum
Age, year	70	12	51	89
Prostate Specific Antigen	6.185	9.221	0.02	100
Postvoid residual urine, ml	35	80	0	1737
Prostate size, gr	63.5	29	24	250

According to documents of patients from ultrasonography of urinary bladder 98 (30.1%) of study participants had urethral catheter or cystostomy and 228 (69.9%) participants did not have, most of them had cystostomy instead of urethral catheter, probably due to large prostate size which has obstructed the prostatic urethra or cystostomy was considered saver than applying urethral catheter for urethral mucosa. 24 (7.4%) of study participants had urinary bladder stone and 302 (92.6%) did not have urinary bladder stone, nine (2.8%) of study participants had urinary bladder diverticula and 317 (97.2%) of participants did not have (Table 2)

Table 2 – prevalence of urinary catheter, bladder stone and bladder diverticula in patients with BPH during 2019 – 2020 (N=326)

Variables	Yes N (%)	No N (%)
Urethral catheter or cystostomy	98 (30.1%)	228 (69.9%)
Urinary bladder stone	24 (7.4%)	302 (92.6%)
Urinary bladder diverticula	9 (2.8%)	317 (97.2%)

In 326 study participants who had BPH, urine culture have been done for all participants routinely, 230 (70.6%) patients were culture negative and 96 (29.4%) patients were culture positive. From 96 positive cultures (29.4%), only 33 patients had antibiotic susceptibility test for antibiotic selection remained 63 patients had only culture reports, because susceptibility test is not done routinely maybe due to economic issues, hence these cultures without susceptibility tests have been omitted from further analysis. In 33 susceptibility test eighteen different species of bacteria were found, The most common pathogen was Escherichia coli (E. coli, 25.3 %), the second most common was Staphylococcus Saprophyticus (12.5 %), the third, fourth and fifth most common pathogens were staphylococcus Epidermidis, Enterobacter Coloacae and Enterococcus Faecalis accordingly (Figure 1).



Figure 1 - Microbial isolates in urine cultures of benign prostatic hyperplasia patients with UTI

From 96 culture positive, in 90 (93.8%) of them have been grown single bacteria gram negative or positive, in 6 (6.2%) of them have been grown more than one type of bacteria in 5 of them were grow two bacterias and only in one case there were three bacterias. In 96 patients with culture positive 54 (56.3%) were gram negative bacteria, 40 (41.7%) were gram positive bacteria and in 2 cases (2.1%) there were both gram negative and positive. The bacterial isolates on susceptibility testing were mostly sensitive to imipenem (93.9%), meropenem (90.9%), tazobactam/piperacillin (88.8%), fosfomycin (84.4%), gentamicin (75.8%), amikacin (69.27%), ceftriaxone (60.6%), levofloxacin (57.6%), ciprofloxacin (48.5%), cefazolin (45.5%), ceftazidime (36.4%) and cefotaxime (33.3%)



Figure 2 – Antibiotic sensitivity pattern among bacterial isolates in 97 urine cultures

Antibiotics to which the isolates were mostly resistant included cefotaxime (66.6%), ceftazidime

(63.6%), and cefazolin (54.5%)



Figure 3 - Bacterial resistant pattern to the antibiotics among bacterial isolates in 97 cultures

The susceptibility of E. coli to common antibiotics is shown in figure 4. As mentioned before

in 12 cultures with sensitivity tests E. Coli was grown.



Figure 4 – Antibiotic susceptibility test for E.Coli

Also a Mann Whitney test was performed and indicated that level of PSA was significantly greater for study participants whose urine culture was positive or had bacteriuria (Mdn = 6.49) than for those whose urine culture was negative or did not have bacteriuria (Mdn = 3.76), U = 8177.5, P = 0.000. The age of study participants was significantly greater for those who had bacteriuria (Mdn = 70) years than those who did not have bacteriuria (Mdn = 67), U = 9569, P = 0.048.

Table 3 - Statistical tests of difference of age and PSA between those who had bacteriuria and those who did not have bacteriuria

variables	Bacteriuria (n=97)	No Bacteriuria (n=229) Test of d		ifferences
variables	Median	Median	Z-value	P-value
PSA level, ng/l 6.49		3.76	-3.765	0.000
Age, years	70	67	-1.978	0.048

There were a weak correlation between prostate specific antigen and prostate size (p=0.044, Pearson correlation 0.111) but this correlation was not significant between age and prostate specific antigen (p=0.54, Pearson correlation 0.107). By performing Chi square test we found significant relationship between having urethral catheter or cystostomy and pyuria, bacteriuria, hematuria and proteinuria. The test results and cross tabulation of urethral catheter with pyuria, bacteriuria, hematuria and proteinuria are shown in (Table 4)

Outcome variables which were tested with urethral catheter or		<b>Cross tabulation</b>	of different factors	Chi square test result	
		Urethral cathe	eter or cystostom	Chi aquara valua	Sig v
cystostom		yes	No	Chi square value	Sig. v
Pvuria	Yes	62	77	05%	0.000
i yurra	No	36	151	9370	
Bacteriuria	Yes	50	47	0.50/	0.000
	No	48	181	9370	
Homotovio	Yes	58	75	050/	0.000
пешацигіа	No	40	153	9370	
Proteinuria	Yes	54	72	050/	0.000
	No	44	156	93%	0.000

Table 4 – Statistical tests of the chi square among the patients having BPH

The test for DM as a risk factor for UTI and pyuria, bacteriuria, hematuria and proteinuria was not significant. And also there were no significant relationship between urinary bladder stone and pyuria, bacteriuria, hematuria and proteinuria by performing qui square tests.

#### Discussion

The prevalence of bacteriuria in our study participants was 29.4% and it was different in many studies. In two studies one pre TURP urine culture with prevalence of 23.5% [19] and other post TURP urine culture with prevalence of 15.5% [20] were reported the prevalence of bacteriuria lower than we reported. While in four other studies on BPH patients bacteriuria was reported higher as 35.6%, 44.7%, 70% and 76.6% respectively than our result [14], [17], [21], [22]

In our study the most common pathogen was Escherichia coli (E. coli, 25%), the second most common was Staphylococcus Saprophyticus (12.5 %), the third, fourth and fifth most common pathogens were staphylococcus Epidermidis (10.4%), Enterobacter Coloacae (9.4%) and Enterococcus Faecalis (7.3%) respectively. In other studies the same like our study the E. Coli was the predominant bacteria responsible for UTI in BPH patients but with higher percentages than our study as 31.81 % [23], 33,3 % [14], 33 % [2], 47.6% [22], 60% [17], while Dybowski et al studied the same study participants in three different periods and the results were almost the same like we found, and E. Coli was the most common organism with 22%, 25% and 27% in three periods respectively [13].

In our study the second most common bacteria in culture positive patients was staphylococcus saprophyticus 12.5%, while in most of other studies the second most common bacteria was Klebsiella species with different percentages like 28.78% Mishra17.3% [14], 15% [2], 8,2% [17], in our study the percentage of all Klebsiella species were 5.2%.

In our study the bacterial isolates on susceptibility testing were mostly sensitive to imipenem (93.9%), meropenem (90.9%), tazobactam/ piperacillin (88.8%) and fosfomycin (84.4%), this finding is nearly the same as Agbugui et al reported; The bacterial isolates on susceptibility testing were mostly sensitive to imipenem (90.5%), meropenem (88.9%), and nitrofurantoin (85.7%) [22] but Delcaru et al reported the susceptibility test of their study participants as follows: The enterobacterial strains exhibited high antibiotic susceptibility rates to fosfomycin (100%), gentamicin (77.14%), nitrofurantoin (75.71%), ceftazidime (74.29%), sulfamethoxazole (62.86%), amoxicillin-clavulanic acid (61.43%), cefuroxime (60%), flouroquinolones (52.86%), and tetracycline (48.57%) [17] which is different from our study and this difference can be due to not testing carbapenem group of antibiotics in their susceptibility tests.

#### Conclusion

Less than one third of BPH patients had UTI (29.4%), E. Coli was the most common microbial cause of UTI in study participants it was the cause

in one fourth of cases (25%), Imipenem group of antibiotic was the most sensitive antibiotics in study participants (93.9%), Cefotaxime was the most resistant antibiotics (66.7%)

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# COMMUNITY UNDERSTANDING, PERCEPTION AND PRACTICES ON INFECTION PREVENTION FROM THE CORONAVIRUS DISEASE (COVID-19): A QUALITATIVE STUDY IN RURAL BANGLADESH

The current study had tried to assess the rural community's understanding, perception and practices on infection prevention to protect from the COVID-19 pandemic.

It is a qualitative study using eight focus group discussions (FGDs) and 40 in-depth interviews (IDIs). Manual content analysis processes were used.

The respondents had good understanding of COVID-19 but had limited knowledge of its spreading, symptom and prevention. Community health workers and adolescents were found to be more aware of COVID-19 issues. Pregnant women and their guardians had limited knowledge and practices on CO-VID-19 prevention. Ignorance and negligence were identified as the major causes of lack of perception and lack of practices on COVID-19 among them. The adolescents acquired many ideas from the internet, peer learning and also from their teachers. The community leaders received knowledge from the news on television and the internet and local authority meetings. All the participants emphasized delivering messages through public announcements and leaflet distribution. The community women had very limited knowledge, perception and practices on COVID-19. Conclusion: Policymakers and health care providers should use common man's language to disseminate the COVID-19 related information. Logistic gaps emerge as the main constraint for preventive measures for COVID-19.

Key words: Corona virus, perception, community, rural, health workers.

# Introduction

Coronavirus Disease 2019 (COVID-19) is an ongoing pandemic caused by Severe Acute Respiratory Syndrome Coronavirus 2 [SARS-CoV-2] [1]. China reported the first case on December 31, 2019. Later the World Health Organization (WHO) recognized COVID-19 as a pandemic on March 11, 2020 [2]. The report shows that the case fatality of COVID-19 is much lower than that of other similar types of infectious diseases like Ebola, Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS) [3]. From 31 December 2019 to 20 May 2020, COVID-19 confirmed cases are 5036018; related death is 326239, and the number of recovered patients is 1,988,644 [4]. According to WHO, the Global mortality rate of COVID-19 is 3.4% and the average count of days from the appearance of the first symptom to death is 14 days [5]. According to the Directorate General of Health Services (DGHS) of Bangladesh, the first 3 cases were identified on March 8, 2020. Then the case number has been increasing gradually. The infection rate stayed low until the end of March, but it saw a steep rise in April. According to the last report on May 20, 2019, total confirmed cases were 26738 out of 203852 tests, overall death was 386, and the total recovered patient number was 4993. Among the COVID-19 positive cases, 68% of confirmed COVID-19 cases were male and 50% were found in the age range between 21-40 years. Among the COVID-19 death cases, 73% were male and 69% were found above 50 years of age [6,7]. WHO Recommended preventive measures including hand washing; maintaining physical distance; avoiding going to the crowded places; avoiding touching eyes, nose and mouths; following good respiratory hygiene; and self-isolation for people who suspect that they are infected [8]. The time from exposure to onset of symptoms is typically around five days, but it may range from 2-14 days [9]. Community people need to be aware of COVID-19 and their pre-

ventive practices [10]. The restriction of the movement of people and goods is one of the major steps to prevent the spread of the COVID-19 [11]. Countries all around the world have adopted staying in the home; physical distancing; washing hands with soap for at least 20 seconds at a regular interval; and practicing cough etiquette as keys to control the spreading of the virus [12]. Bangladesh faces a significant challenge in keeping physical distance to prevent spreading the virus, due to its high population density [9]. Bangladesh has taken several initiatives at the earlier stage of the pandemic after confirmation of COVID-19 cases in the country. These include declaring general leave since March 26 which is continuing, closure of all academic institutes, stopping all public transports, and strict lock-down in some of the areas/districts as required [13-18]. The country developed guidelines on infection prevention and control, and messages/posters/leaflets with preventive messages. These are being regularly circulated through print and electronic media [19]. Awareness-raising events are organized through the representatives from the local government, local law and enforcement department. Hotline numbers have been assigned to respond to any questions related to COVID-19[20]. Since Bangladesh is a developing country and over 70% of its population live in rural settings [21], there are difficulties in disseminating correct information and increase their practices. This study had tried to assess the community understanding, perception and practices on infection prevention to protect from the COVID-19 pandemic.

# Materials and methods of research

A qualitative study was conducted during the period in October 2020 in the Moulvibazar district of Bangladesh. The focus group discussion (FGDs) and in-depth interviews (IDIs) were conducted with different community groups. A guideline was developed covering community perceptions, knowledge and practices on prevention from COVID-19.

A total of eight FGDs were conducted with different community groups. FGD participants included pregnant women, guardians of pregnant women, community healthcare workers (HCW), community leaders, adolescent girls, adolescent boys and eligible couples. For IDIs, the participants included facility-based health care providers and community women. The FGDs were conducted physically and IDIs were conducted through mobile phone-based interviews.

Six data collectors were recruited for information collection. A guideline was developed by the investigators for conducting the FGDs and IDIs of the study. Online training was provided to data collectors for qualitative data collection. FGDs and IDIs were not intended to be representative of the population under the study; hence the respondents were not selected randomly. They were selected according to the characteristics which are important for this study and according to the participants' willingness for participation.

The investigators reviewed the documents, finalized the assessment design and tools for the IDIs and FGDs. A research team of six data collectors was recruited and trained for qualitative data collection. The investigators also established field level communication for the conduction of the study. The guidelines were field-tested before data collection. The guidelines contents included perception; knowledge; practices and recommendation on COVID-19 among different stakeholders (community peoples, service providers and service recipients) with different points for discussion [Table 1].

Tools	Areas	Points for discussions		
		Understanding of Coronavirus and COVID-19		
		How did they come to know about COVID-19 the first time		
	Perception and knowledge of	How COVID-19 spreads		
	COVID-19	nowledge on the symptoms of COVID-19		
		Knowledge on prevention of COVID-19		
FGD an	1	What to do if anyone has symptoms of COVID-19		
IDI	Practices on prevention of	Hand washing		
		Using face masks		
	COVID-1)	Practicing social distance		
	D 1.C	Ways to disseminate COVID-19 related information in community		
	Recommendation on	From whom it is best to know further about COVID-19		
		Understanding on what suggestive measures can be taken		

Table 1 - Points for discussion about the qualitative data collection

Eight FGDs were conducted with 67 participants of seven groups of peoples. In FGD sessions each participant was asked a question in turn and all participants reacted to comments made during the conversation. The research team ensured that each FGD session works properly with the discussion of the merits and demerits, good and bad practices, ways of improvement and all other relevant and pertinent issues related to the concerned subject.

Each session consisted of 8-10 participants. FGDs were conducted at a convenient time and place for the participants. The sessions as per the discussion guideline prepared beforehand covering all the concerned issues. One from the research team moderated the session and another took notes of discussion to identify the who-said-what-in-what context. The audio record of the discussion was also kept with the participants' consent. The discussion was conducted in a neutral setting and the session moderator kept the discussion within the framework of the topics of concern.

IDIs were conducted over the mobile phone with facility-based service providers (family welfare visitors, midwives, community health care providers, and senior staff nurses) and community women in Moulvibazar. IDIs involved not only asking questions over the mobile phone but documenting responses completed with intense probing for deeper meaning and understanding of the responses. The interviewer recorded mobile phone conversations with respondents' permission. A total of 40 IDIs were conducted by the trained research officers with 30 community women and 10 health service providers. Each IDI required 10-15 minutes of conversation [Table 2].

Table 2 – Participant	details of the FGD and IDIs
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Data Collection Tools	Number of Participants	Age of the respondents	Study Population (No of participants)
Focus Group Discussion (FGD) guideline	Total 8 FGDs, 67 participants	18-54 years	<ul> <li>FGD1: Pregnant women (10 participants)</li> <li>FGD2: Guardians of pregnant women (7 participants)</li> <li>FGD3: Community health workers (8 participants)</li> <li>FGD4: Community health workers (9 participants)</li> <li>FGD5: Community leaders (10 participants)</li> <li>FGD6: Adolescent girls (8 participants)</li> <li>FGD7: Adolescent boys (7 participants)</li> <li>FGD8: Eligible couples (8 participants)</li> </ul>
In-depth Interview (IDI) guideline	Total 40 IDIs through phone call	18-39 years	Facility based health providers (10) Family Welfare Visitor [FWV] (1) Midwives (5) Community Health Care Providers [CHCP] (2) Senior Staff Nurses [SSN] (2) Community women (30)

The investigators were responsible for overall supervision and monitoring of the research and they also provided feedback during data collection. The field plan with task distribution was done at the beginning of the study. The investigators reviewed all activities and outputs of each day, discussed with the team members about the issues, provided appropriate feedback to ensure quality and solve problems during fieldwork and readjusted the plans accordingly to finish the job in time.

An audio recording of IDIs and FGDs were transcribed independently by the investigators and compared for accuracy. Intellectual transcription was done with back to back translation. Investigators reviewed and analyzed the data through making table and familiarization of the data by reading, re-reading and developing ideas for codes. Once all data were coded, they were categorized based on themes and sub-themes. Then data were interpreted, analyzed and reported. After sorting and categorizing the responses, excerpts from the transcripts were chosen to be illustrated as summary statements, which were also used to validate the findings. The data were analysed through the manual content analysis process.

#### Ethical issue

The national ethical review committee of CIP-RB has approved (CIPRB/ERC/2020/20) this study. Written and verbal consents were received from each of the respondents before the interview, as applicable for physical and online meetings.

# Result

The study revealed that the respondents' understanding of COVID-19 was found good but had limited knowledge on spread, symptom and prevention of COVID-19. The ignorance and the logistic gaps were found to constrain in hand washing, using the facial mask and practicing social distance persisted in the community for proper practices.

FGD findings showed that Community health workers and adolescents were found to be more aware of COVID-19 issues. Pregnant women and their guardians had limited knowledge and practices on COVID-19 prevention. Ignorance and negligence were identified as the major causes of lack of perception and lack of practices on COVID-19 among them.

The adolescents acquired many ideas from the internet, peer learning and also from their teachers.

The community leaders received knowledge from the news on television and the internet and local authority meetings. All the participants emphasized on delivering messages through public announcements and leaflet distribution.

IDI findings presented that the facility-based providers had good perception and knowledge on COVID-19 including the symptom and prevention of the disease. The logistic gap was raised to hinder the proper practices. The mask, hand gloves, soap, hand sanitizer and tissues need to be available among both the service providers and service recipients. This group also emphasized that the HCWs need to be trained for counseling the general population about the disease. The community women had very limited knowledge, perception and practices on COVID-19 [Table 3].

Major findings			
Corona is a virus cause disease/ COVID-19 is a viral infection/disease			
• Ignorance about the disease and negligence on related issues			
• Lack of knowledge on the COVID-19 symptoms			
• Knew about necessity of hand washing but did not know the duration and interval of hand washing			
<ul> <li>Masks are useful to prevent the transmission of germs through air</li> </ul>			
Social distancing and the information related to it			
Washing hands with soap or ash			
Washing hands more frequently than previous times			
<ul> <li>Did not practice hand washing for 20 seconds at every 20 minute interval</li> </ul>			
• Less use of face masks due to unavailability and inability to buy			
• Did not practice due to discomfort			
Maintaining distance from ill people			
• Didn't maintain distance to mix with other people/Did not practice social distancing while being			
among many people			
<ul> <li>Placing elbow or piece of cloth during coughing or sneezing</li> </ul>			
Avoid spiting in open places			
<ul> <li>Knew about cough etiquette but could not remember to practice</li> </ul>			
Awareness among all community people			
• Community health workers deliver the awareness message in the best way			
Micking/public announcement and leaflet distribution			

Table 3 – Summary findings of FGD and IDIs

The results covered each of the areas including perceptions, practices and recommendations from the community people, service providers and service recipients on COVID-19 issues through FGDs and IDIs.

## Perception and knowledge on COVID-19

The findings of the perception of COVID-19 include the perception of the community people, service providers and the community women. Among the community women, 90% of the respondents lacked general ideas on COVID-19. The information mainly came from the young educated respondents in comparison to others.

# **Understanding on COVID-19**

The majority of the respondents from all categories knew that Coronavirus is a virus that causes the disease to a human. The adolescent groups were able to mention that COVID-19 is a viral disease. Though the majority of the respondents of community women heard the term Coronavirus they were not aware of this issue. Some of the participants found the term new for them. According to them, it may not be a serious disease in Bangladesh, but it is for other countries like China. The majority of the respondents did not consider this issue as a serious concern, where some of the participants expressed their anxiety about this disease.

«COVID is a viral disease. The disease occurred in China. In Bangladesh, there is a low risk to occur in these diseases. So we need not be anxious about this disease» – P3, FGD8, Eligible couple

«I know corona is a virus that causes death to a human. This disease transmitted from the people who came from abroad. The infected people suffer from coughing, fever and throat pain»- P2, FGD6, Adolescent girl

«I heard that corona is a virus. One of my neighbors informed me. I never heard about this disease earlier. But I heard that this disease is very dangerous for human».- P14, IDI, community women

«Corona is a contagious virus that has can infect anyone easily. Elderly people, in particular, suffer from seizures».- P1, IDI, Family welfare visitor (FWV)

# How did they come to know about COVID-19 the first time?

The community people including pregnant women, their guardians, community leaders, and adolescents heard the term mostly from television, social media platforms and other community people. The pregnant women were informed of this mostly from their adolescent family members who had heard from their friends. The community leader mentioned getting the information from meetings and television. The HCWs learned from social media, television and the doctors and health managers of their facilities.

«I heard that a new disease came to our country, named CORONAVIRUS from one of my neighbors. He said this disease can kill people. But we had no opportunity to know the detail on this». – P5, FGD1, Pregnant woman

«I heard about the disease from the internet and my friend. This disease can be transmitted from one person to another.» – P7, FGD6, Adolescent girl

«I heard about the disease from my husband. He learned it from the market. We have limited sources to learn as we do not have television or radio. If public announcements were conducted on this issue then we can learn more about it», – P23, IDI, Community woman

«I learned about this from Facebook. This is an interstate problem. Many countries have to go under lock-down for this. It cannot be said today about what will happen to our country in the next five days.»- P8, IDI, Community Health Care Provider (CHCP)

# How COVID-19 spreads

The majority of the community leaders and adolescents mentioned about the sneezing/coughing of infected individuals was the main route of contamination. The community women had very poor knowledge of the transmission/contamination process of this virus. The health care providers had more ideas on the process of contamination than the others. The pregnant women had no ideas on this, but their guardians mentioned that it might occur for misfortune and bad luck.

«I had no clear idea of the process of contamination. I heard that it can be contaminated through the coughing and sneezing of an infected person.»-P2, FGD5, Community leader

«Usually one can be infected by touching and coughing. If he has fever, cold, cough and sore throat, he will assume that he is infected with the virus.»- P6, FGD3, Community health worker

«It might occur if our fate is not good. It is the will of God. We have nothing to do.»- P19, IDI, Community women

«Sneezing and coughing of infected individuals, coming to contact with other people and joining mass crowds/gatherings and public transportation were the main ways of contamination of COVID-19»- P2, IDI, Midwife

#### Knowledge on the symptoms of COVID-19

According to the adolescents, sneezing, coughing and throat pain was the major symptoms of COVID-19. Pregnant women and their guardians had limited knowledge of the symptom. Community leaders could mention that the sneezing, coughing, common cold, fever were the main symptoms of this disease. The majority of the Community women did not know about COVID-19 symptoms. Mostly facility health workers and community health workers responded that the symptoms included fever more than 1000F, dry cough; respiratory distress and pain in the throat.

«I heard that dry cough with 4 to 5 days duration and then diarrhea is the symptom of COVID-19. It can be spread through sneezing»- P7, FGD2, Guardian of a pregnant woman

«Coughing, sneezing and throat pain are the main symptoms of this disease. If anyone is infected, then he needs to keep himself separated otherwise others may be contaminated as well». – P5, FGD8, Eligible couple «I heard that coughing and fever occurred in COVID-19, but how these can confirm this disease from the common cold is not known to me. It is confusing with other disease symptoms»- P30, IDI, Community woman

«If one experiences sneezing and coughing with fever, he needs to keep himself in isolation for 14 days for observation. If one holds breathing for 5 seconds, it can be understood either he has respiratory problems. Also, it can be ascertained whether or not it is CORO-NA infected through IEDCR» – P6, IDI, Midwife

# **Knowledge on prevention of COVID-19**

The community women of Moulvibazar district could not mention any process to prevent COVID-19. Some of them mentioned that cleanliness at all times can prevent any disease. In Habiganj, the community women mentioned that washing hands is one of the ways to prevent COVID-19 but could not say how to wash hands and the ideal duration for washing hands. Pregnant women, their guardians and community leaders mentioned that hand washing needs to be practiced at every 20 minutes for the prevention of COVID-19. Some of the health workers mentioned that repeatedly hand washing, maintaining physical distance, using tissues during coughing and cleaning were important for the prevention of COVID-19.

«Mask can prevent the transmission of germs from one to another through the air. Hand washing is also very important after handshaking with others or handling money»- P6, FGD7, Adolescent boy

«Everybody should use masks, and be alert to prevent COVID-19. Besides, religious bigotry and superstitions need to be abolished. Awareness activities can be strengthened to prevent contamination to some extent»- P3, FGD5, Community leader

*I have no idea how to prevent this disease. I think cleanliness can prevent any type of disease. –* P28, IDI, Community woman

«The main obstacle to prevent COVID-19 is the continuation of migrations and lack of awareness. It is not possible to prevent the disease unless public gatherings are avoided. We need to obey the government directives to control COVID-19, like staying home without special needs.»- P4, IDI, Midwife

# What to do if anyone had symptoms of COVID-19

The majority of the participants mentioned taking the patient immediately to the hospital. Some of the facility health providers mentioned about immediate contact/consultation with physicians and IEDCR, and isolation. Some of the adolescents and community health workers mentioned that staying home, keeping a distance from other people and using masks while being infected are very important.

«The patient needs to contact the doctors and nurses in the adjacent facilities, in case anyone is infected. The patients need to get admitted in the adjacent hospital»- P8, FGD5, Community leader

«Proper use of the mask must be ensured. In the case of sneezing, we generally follow some rules; so that no one else faces any problem. Following the general rules announced by the government is a way toward safety.»- P7, FGD7, Adolescent boy

«Everyone needs to keep a distance from the infected people and inform our community health workers about the ailment. We advise a suspected individual to remain in isolation for 14 days.» – P16, IDI, Community woman

«In any disease, we would usually send the patients to Upazila Health Complex and District Sadar Hospital. But we have no direction in case of this disease. As it is highly contagious, so it is better to communicate with hotline number and maintain the rules of isolation»- P7, IDI, CHCP

#### **Practices on prevention of COVID-19**

Practices of the prevention of COVID-19 include the practices of the community people, the service providers and practices of the community women. The respondents expressed whether they practiced hand washing, wearing face masks, taking precautions during coughing and sneezing, and maintaining the social distance. None of the participants was found to maintain all the precautionary measures of COVID-19. The health workers were found to maintain a limited number of preventive measures. The adolescents were found to practice at least one precautionary measure. None of the community women maintained any precautionary measure. The majority of the community people did not practice due to negligence.

# Hand washing

The Adolescent group mentioned that they used to practice washing hands with soap before and after meals. But they did not practice any other specific process of hand washing for COVID-19.

«We washed our hands before meals. This was enough to kill all organisms which cause diseases. Nothing else needs to be practiced for COVID-19»-P5, FGD6, Adolescent girl

I know I need to wash hands for 20 seconds every 20 minutes interval but we did not have enough soap to use for hand washing. We need special support for practicing this important issue»- P9, FGD4, Community health worker
«Although I know that hand washing with soap is essential but I could not practice due to my hectic involvement with other domestic tasks». – P12, IDI, Community woman

«There are 6 steps for hand washing. Another step has recently been added with these to wash hands. These 7 steps are to be followed at a scheduled time. I am following these and I want to disseminate the knowledge with others if I get the chance.»-P6, IDI, Midwife

#### Using face masks

According to the adolescent group, none should cough or sneeze in an open place and they mentioned using elbow or cloth during sneezing or coughing. They tried to practice it. But according to them, their community did not practice it. The community people heard about using face masks, but it was not available. So, they could not use it. The majority of them did not emphasize on using face masks. Adolescents were very aware, and they practiced using face masks. Some of the community leaders used these and motivating others too. The community women did not practice this.

«We occasionally use the masks as the disease cannot spread if we use masks. We cannot always use it because the mask is not very available in our community.» – P5, FGD3, Community health worker

«I heard that masks need to be used only by infected people. So I do not use this. I also feel uneasy to use the mask.» – P4, FGD2, Guardian of a pregnant women

«The government is unable to supply masks to the Community Clinics. So we have to manage it by ourselves. Health care providers must first ensure PPE supply to prevent Coronavirus disease»-P7, IDI CHCP

«I know the importance of using masks, but we do not have sufficient supply. The main obstacle to prevent COVID-19 is the lack of protective equipment and training. COVID-19 can be prevented if you can ensure the necessary training and supplies for health care providers» – P5, IDI, Midwife

#### **Practicing social distance**

Adolescents maintained to keep a distance from an infected individual but did not practice any distancing among themselves. The measurement of distance was not known to them. The actual measure of physical distance maintenance could not be found from any participant. Some health care providers mentioned that 3 feet distance is essential were some others mentioned the distance to be 3 meters. «We have to maintain three meters distance from the affected people but there is no need to maintain distance among the healthy people»- P2, FGD1, Pregnant woman

«We know the physical distance needs to be maintained but it is difficult to practice. We have to go to the market for shopping where gathering occurs. If everyone can be made aware of this then it can be practiced in reality». – P4, FGD5, Community leader

«I practiced keeping distance with any infected individual, but I do not know how much distance needs to be maintained»- P11, IDI, Community woman

«It is not possible to keep the distance from patients. Moreover, there is a lack of necessary equipment for our safety. Because of this, we are taking risks in providing health care.»- P1, IDI, FWV

#### **Recommendation on controlling COVID-19**

Recommendation part of the result section includes recommendations from the community people, recommendations from the service providers and recommendations from the community women for the prevention of COVID-19.

# Ways to disseminate COVID-19 related information in the community.

According to the adolescents, the school programs, awareness meetings, public announcements, distribution of the leaflets/brochures/posters made them and their community awareness about the prevention of COVID-19. Pregnant women and their guardians mentioned that COVID-19 should be discussed on courtyard meetings and brochures/posters can be helpful for easy and clear understanding. The community leaders mentioned that more announcements should be available on TV, radio and also on social media platforms. The Government and NGOs should also have special initiatives on this issue.

«I have limited knowledge of COVID-19. So how can I share with my community people regarding this issue? So, the GoB and NGOs need to be forward to aware us regarding this issue.»- P9, FGD5, Community leader

«Public announcements and leaflet distribution in the rural areas are the best ways to deliver the message among us. The local language during the announcements will make it easier for us to understand.» – P8, FGD1, Pregnant woman

«Public announcements can be done in the area to spread the preventive message among the general population. It is also possible to preach through the mosque's imam.»- P14, IDI, Community woman «The main obstacle to prevent COVID-19 is the lack of education and awareness. To spread the message to the common people, it is necessary to arrange village-to-village public announcement and, extensive public awareness activities.'- P8, IDI, CHCP

# From whom it is best to know further about COVID-19

The majority of the respondents mentioned that the health workers in their community were able to deliver the messages on COVID-19 more comprehensively. They could also share their problems with them easily.

«We, the community people, depend on the community health workers. So, it will be best for us if they can share COVID-19 related information with us according to our own understanding.» – P5, FGD2, Guardian of pregnant women

«If home based services are made available by the government and NGOs, then the community people can be more aware on COVID-19. Video shows could also be helpful»- P10, FGD5, Community leader

«We can learn easily through our peers and from our teachers. If the internet can be made available for us, then we can learn all the information much easily». – P3, FGD7, Adolescent boy

«We need training from the experts on this disease. Then we can easily share the knowledge with others through counseling or providing care»- P10, IDI, Senior Staff Nurse (SSN)

# Understanding what suggestive measures can be taken.

According to the respondents, the follow-up of the government order is very important. The HCWs mentioned that the Government issued the order to wash hands at every 20 minutes interval and to maintain social distance by staying at home. These orders need to be maintained strictly to control COVID-19. Community people and community women could not mention any means to control COVID-19. They emphasized on their own and community awareness for controlling the disease

«Everyone should be aware that during this pandemic, nobody should go outside without any emergency. Everyone needs to use face masks when outside. One should not shake hands with others.»-P5, FGD3, Community health worker

«Cleanliness helps prevent COVID-19. There is no alternative to awareness. Everyone should follow the general rules as his responsibility. We do not need to focus on the resistance of the developed country. We need to take the necessary steps given our overall situation». – P8, FGD5, Community leader

«The main obstacle to prevent COVID-19 is the lack of awareness among the general population, lack of necessary equipment for healthcare providers, no PPE. Apart from these, it is possible to prevent Corona by announcing the closure of companies and big supermarkets.» – P9, IDI, Senior Staff Nurse (SSN)

«We need to obey the government directives to control COVID-19, and we all should stay at home, unless any special needs.»- P3, IDI, Midwife

#### Discussion

The perception of community people about the risks, symptoms, management and prevention of COVID-19 was explored in this study. The major findings of the study revealed included limited knowledge on spread, symptom and prevention of COVID-19 among the respondents. Hand washing, using a facial mask and practicing social distance were not found practiced in the community due to ignorance and unavailability of the logistics.

COVID-19 or Coronavirus Disease 2019 is the latest global threat that the world has been encountering, which was recognized in December 2019[22]. The scientists joined in to identify the cause of this contagious disease to be SARS-CoV-2[23]. This novel Coronavirus is structurally related to the virus causing Severe Acute Respiratory Syndrome (SARS) [24], hence the name. Similar to previous two preceding of Coronavirus related infectious diseases as Middle East Respiratory Syndrome (MERS) and SARS [25], COVID-19 also poses a critical challenge for communities all around the world, along with the emergence of newer encounters of public health initiatives, the urgency of researches and curative and preventive modalities [26].

While observing the disease trend at the beginning of the disease outbreak in Hubei province of China, epidemiology shows that the patient's age was averaged for 59 years, with higher morbidity and mortality among the elderly [27]. Most of the patients were male, and there was no patient identified with COVID-19 below 15 years of age [26]. However, as the disease spread to 216 countries of the world until now [28], the patient epidemiology has been altered. Patients, irrespective of their ages, are being diagnosed with COVID-19. Even newborns are getting infected all over the world [29,30].

If the timeline for COVID-19 is reviewed, the China Health Authority alerted the WHO about cases of pneumonia with unknown origin on December 31, 2019. The earlier cases were reported within the Wuhan city inhabitants living around the Huanan Seafood Wholesale Market, although there were cases who had no exposure to this place [31]. WHO identified a novel Coronavirus, later named as SARS-CoV-2 [32] from the patient sample [33]. The organization declared the disease as a Public Health Emergency of International Concern (PHEIC) on January 30, 2020 [34]. On March 11, 2020, WHO declared COVID-19 as a pandemic [35]. Bangladesh has first identified three patients with COVID-19 on March 8, 2020.

SARS-CoV-2 is a novel human-infecting Beta coronavirus [36]. Bats are likely to be the origin of the virus, however, further research is necessary to confirm whether COVID-19 is transmitted directly from bats or through any intermediary host [37,38]. When the human transmission and sustenance of this virus were confirmed [39,40], it has been observed that respiratory droplets are the main route for it [38]. Newer studies have suggested fecal-oral [41], and possible aerosol transmission [42], although further studies are necessary for confirmation. Additionally, a newborn of a COVID-19 positive mother was diagnosed after 30 hours of her birth [43]. thus suggesting vertical transmission of the SARS-CoV-2. These confirm that any individual of any age and sex can be infected with SARS-CoV-2 at any time, so universal precaution is necessary.

Response to COVID-19 outbreak for curative purpose is limited to symptomatic treatment with organ support, including respiratory ventilation in intensive care for seriously ill patients [44], as no vaccine or antiviral treatment for human and animal Coronavirus infection is available [45]. Current treatment modalities for general care is prescribed as bed rest and supportive treatment with antiviral therapy, antibiotics and immunomodulating agents [46-47], multiple organ function and respiratory support, bronchoalveolar lavage (BAL), blood purification, extra corporal membrane oxygenation (ECMO) [48] and convalescent plasma therapy [49]. Treatment is given to the COVID-19 patients based on triage, and all these modalities are expensive, unavailable and relatively time-consuming for the general population.

COVID-19 is a highly contagious communicable disease affecting all population [30]. At present, there is no vaccine available to prevent COVID-19. WHO announced that developing an effective vaccine will take at least 18 months, even after ensuring funding and public interest in this endeavour [50]. So, community prevention is still the best method to stop COVID-19 outbreak. To observe the effectiveness of disease prevention strategies, cohort studies are important in well-defined settings such as schools, workplaces, or community places [51]. Information on COVID-19 risk, symptoms, burden and attack rate, the severity of the epidemic, hospitalization, death [52] and its prevention can be disseminated among the general population through various measures. Household surveys have proven to be a superior source of data regarding the rate and chances of viral transmission [53]. Considering the importance of such studies, our qualitative assay was conducted to see the community perspective of COVID-19 prevention.

WHO and all other health organizations have emphasized on maintaining hand and respiratory hygiene and adhering to social distancing protocol to prevent COVID-19 transmission [54]. A total of 67 participants from the community and 40 IDIs among healthcare workers (HCW) have shown a fair idea of the disease pathogenesis and signs/symptoms of COVID-19. HCWs have received multiple sessions of training from different local government and privet authorities of Bangladesh which ensures relatively higher technical knowledge within this group. Community leaders accessed the knowledge using both news mediums and the local government initiatives. However, pregnant mothers and other community women lacked information about COVID-19.

The effectiveness of electronic media, social media, online platforms, and television to circulate information of a contagious viral disease is observed among the adolescent group. This might be a very informative and appropriate field of study to venture into the scopes of using such platforms for spreading information to the mass population.

Unless the messages are delivered to community people of all ages and sexes, a communicable disease such as COVID-19 prevention gets much harder. Our study has observed that many people do not comprehend the danger of Coronavirus transmission in Bangladesh. They would rather dismiss the probability of infection to foreigners or people coming from abroad. An effective way of communicating about the disease has come up through our IDIs, which are public announcements.

Community-women are mostly in charge of household cleanliness and food preparation in Bangladesh. Unfortunately, this group is the most negligent about the spread and danger of COVID-19. Pregnant mothers are always at risk for communicable diseases. As it is yet to be confirmed whether vertical transmission of SARS-CoV-2 is possible or not, it is much required to take preventive measures for them. Higher effective methods for preparedness for disease prevention are necessary for pregnant women and their caregivers. Courtyard meetings, in-person visits and counselling can be useful for the dissemination of knowledge among these groups of people.

Except for the HCWs, the majority of the study population lacked proper knowledge on maintaining hand and respiratory hygiene and social distancing. COVID-19 preventive practices also seemed to be very low among the participants; however, the adolescent group was relatively more aware and interested to adhere to the practices of wearing masks, ideal hand washing, maintaining cough etiquette, and social distancing. Unavailability of the masks and training on hand washing practices and cough etiquette might also be a reason for lack of interest in practicing these preventive measures. Technical knowledge regarding social distancing and all preventive measures require to be increased among the community people. Especially about the ideal hand washing practices and cough etiquette.

Community awareness about any communicable disease is very important. It is even more vital in case of a highly contagious disease like COVID-19. Distribution of informative leaflets, stickers and microphone announcements are ideal methods for that. Religious congregations can also play an imperative role in the dissemination of knowledge and information on COVID-19. However, strict government measures regarding cleanliness practice and social distancing through lock-down are esteemed as essential in the prevention of COVID-19.

#### Conclusion

The initiatives taken in Bangladesh to prevent the spread of COVID-19 and to reduce its harms seem to be effective. However, technical knowledge regarding preventive measures and proactive participation in protecting others is still disappointing, especially among the women in the community. More in-depth studies from other cultural context require to be conducted on the effectiveness, emergence and usefulness of newer mediums of information dissemination. Effectiveness of the current measures could be observed following the decline of the pandemic through the number of affected individuals and deaths among the rural communities. The study suggested that adolescent involvement can be a very effective measure towards any positive social movement regarding behavior change for betterment.

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# ASSESSMENT OF VITAMIN D STATUS AND RESPIRATORY DISEASE RISK FACTORS IN CHILDREN

The diversity of the effect of vitamin D on the body is determined by the discovery of vitamin D receptors on a variety of tissues (40 tissues or more) (Wimalawansa S.J., 2018). However, to date, the diversity of the effect of vitamin D on the body in childhood with diabetes mellitus, cardiac pathologies, the effect on immune processes, malignant formations has not been fully investigated. The importance of vitamin D in the formation of the immune system and anti-infective protection in a child is being studied. Indications for diagnosis and correction are being developed, therapeutic and preventive effective doses of vitamin D for children are calculated (Zakharova I.N., 2017). Therefore, the problem of vitamin D deficiency in children with respiratory diseases has determined the purpose of the study to date. To study risk factors, vitamin D availability in children, the effect of hypovitaminosis on the course and severity of respiratory diseases.

Prospective study of patients of the Department of pulmonology of the DGKB No. 2. 75 patients aged from 1 month to 5 years. I (main) group – 50 children with a low content of vitamin D (25-hydroxyvitamin D) in the blood and II group (control) - 25 children with a level of vitamin D (25-hydroxyvitamin D) in the blood within the normal range.

In the study of vitamin D availability in children with respiratory pathology in 40% of children under the age of 1 year of the main group, vitamin D was determined at a deficiency level of  $15.63 \pm 1.71$  ng/ ml. In breastfed children without additional vitamin D supplementation, 40% of children were deficient. In the patients of the main group, 40% of mothers suffered from chronic diseases of the gastrointestinal tract. In the control group, only 8% of mothers were found to have morbidity.

Key words: children, pneumonia, bronchitis, vitamin D, risk factors.

## Introduction

It has been shown over the past decade that a sufficient amount of vitamin D maintains healthy bones and muscles, and is also important for various diseases prevention [1, 2].

According to the large-scale researches conducted in the Russian Federation, RODNICHOK-1 and RODNICHOK-2 34% and 42% of the surveyed young children, respectively, were deficient in the vitamin D supply, with 18% that were deficient badly, and only 34% children under study had normal levels of vitamin D [3].

It has been proven that the physiological effects of vitamin D are divided in two types, genomic and non-genomic. The genomic type is an effect on a genome (mitosis, DNA repair, chromosome rearrangement), an impact upon polypeptide chain biosynthesis, immunity, embryo formation and development, and upon metabolism. The non-genomic type of vitamin D effects is identified by its impact on VD-binding proteins. 1,25(OH)2D3 has important immunomodulatory effects, namely strengthening of innate immune system and inhibition of adaptive immune responses related to increased synthesis of interleukin IL-4 by T-helper-2 lymphocytes and upregulation of regulatory T lymphocytes.

In fact, different types of immune cells (dendritic cells, macrophages, T- and B-lymphocytes) express VDR, and most of them are able to synthesise calcitriol through an independent regulatory pathway, reacting to a range of pro-inflammatory agents, such as bacterial lipopolysaccharides and tumour necrosis factor alpha [4,5].

This variety of biological effects demostrates the potential to prevent and treat various childhood diseases. So far, the discovery of calcitriol receptors on the cells of the human immune system and the ability of mononuclear phagocytes to generate 1,25 (OH)2 D3 has been a great contribution to the study of the effects of vitamin D on immunity [6]. For long, vitamin D has been considered to be essential for stimulating monocyte differentiation, activating phagocytosis in macrophages and increasing the production of antimicrobial peptides. But later it was proven that the interconnected activity of the other cells was also related to vitamin D; the immunomodulatory effects were identified, which normalised the Th1/Th2 ratio in healthy newborn infants [6]. It has also been found that vitamin D supplementation in babies in their first year of life increases cellular immunity options. However, the vitamin D levels impact on the severity of respiratory disease remains underesearched. Gombart A.F., Borregaard N., Koeffler H.P. (2005) concluded that the group of children with low levels of 25(OH) D had more frequent venipuncture, ventilator use and antibiotic therapy than the group with higher vitamin D levels [7]. Patients with vitamin D levels lower than 30 ng/ml were more vulnerable to severe illnesses caused by respiratory infections, and had an increased need in reducing hypoxemia [8,9,10,11].

Currently, there are recommendations from various countries for a prophylactic dose of vitamin D in children: 1000 IU/day, with 1500 IU recommended especially to children from one to three years of age, while the dose of 1000 IU/day is recommended to 1-6 months infants from the European North, while 1500 IU is a recommendation to those from 6 months to 18 years old [12,13]. Thus, nowadays there is a growing interest in the diverse functions of vitamin D, particularly in its positive effect on anti-infective immunity thanks to the activation of antimicrobial peptides.

The purpose of study is to research the risk factors, vitamin D status in children and the hypovitaminosis impact on the course and severity of respiratory diseases.

The present study was approved (Minutes № 8 of December 5, 2019) at a meeting of the Local Ethical Committee of JSC «Kazakh Medical University of Continuing Education».

#### Materials and methods of research

A prospective analysis were carried out during the study. The children were included in the study by the criteria of being the pulmonology department patients in Children's City Clinical Hospital #2 regardless of gender. The study exclusion criteria were as follows: intake of vitamin D in any form during the last six months before the study as well as genetic syndromes, mental development disorders, active rickets, hepatic and/or renal dysfunction, intrauterine development delay, malnutrition of grade 2-3, and malabsorption syndrome.

The study was conducted in two phases. The first phase involved a retrospective analysis of the patient records, and the second phase was a prospective study of the patients in the pulmonology department of CCCH#2. In a prospective study, 75 patients between 1 month and 5 years of age were selected according to the inclusion and exclusion criteria. The patients were split in groups, where Group I (main group) was of 50 children with low blood levels of vitamin D (25-hydroxyvitamin D) whereas Group II (control group) had 25 children with blood levels of vitamin D (25-hydroxyvitamin D) within normal limits.

Age group	Number of surveyed children				
	Main	group	Contro	l group	
	абс.	%	абс.	%	
1-12 months	20	40	10	40	
1-3 years	18	36	8	32	
3-5 years	12	24	7	28	
Total	50	100	25	100	

Table 1 – Age distribution of children included in the study

As is shown in Table 1, 76% of children in the main group and 72% of children in the control group

were under 3 years of age, being the most vulnerable group for respiratory disease.

The ratio of boys to girls in the main group was 24 (48%) and 26 (52%) respectively. There were 11 (44%) boys and 14 (56%) girls in the control group. The informed consent form to participate voluntarily in the study was obtained from the guardians/legal representatives of the surveyed children.

The 25(OH) D in the blood was found in order to study the blood levels of vitamin D in the children. Blood samples for vitamin D were taken once in 75 patients (of both main and control groups).

We examined vitamin D status in children with respiratory disease (table 2).

Nosological form	Value	Survey	ed group
		Main	Control
Acute bronchitis	abs. number	9	11
	%	18,0%	44,0%
Acute obstructive bronchitis	abs. number	13	6
	%	26,0%	24,0%
Acute tracheitis	abs. number	1	1
	%	2,0%	4,0%
Acute bronchiolitis	abs. number	1	0
	%	2,0%	0,0%
Unilateral focal pneumonia	abs. number	12	5
	%	24,0%	20,0%
Unilateral focal-drainage pneumonia	abs. number	5	0
	%	10,0%	0,0%
Bilateral focal pneumonia	abs. number	5	2
	%	10,0%	8,0%
Bilateral focal-sprain pneumonia	abs. number	2	0
	%	4,0%	0,0%
Destructive pneumonia	abs. number	2	0
	%	4,0%	0,0%

 Table 2 – Nosological forms of children in the main and control groups

Children in the main group were found to have more severe forms of respiratory pathology. Thus, in the main group the destructive pneumonia made 4%, while in the control group no such cases were registered. Focal pneumonias were more frequently diagnosed in the main group, whereas no such forms of pneumonia were detected in the control group (with normal vitamin D content). No cases of acute bronchiolitis were detected in this group either, while in the main group patients with acute bronchiolitis accounted for 2%. Focal pneumonias were more common in the main group: bilateral 10%, unilateral 24%. Focal pneumonias in the control group were detected in 8% and 20%, respectively, and all the cases were uncomplicated.

After identifying the vitamin D level, cholecalciferol preparations were prescribed to the patients with low vitamin D level (the main group). The dosing of vitamin D preparations for the low blood levels correctoion was carried out according to the National Programme «Vitamin D insufficiency in children and adolescents in the Russian Federation: current approaches to correction».

The children with vitamin D blood levels lower than 10 ng/ml were given 4000 IU/day, those with less vitamin D than 10-20 ng/ml got 3000 IU/day, and the ones with 20-30 ng/ml had 2000 IU a day [14]. In a second step, a blood test was performed a month later in the main group, and the efficacy of the selected dose of vitamin D was assessed.

The statistical data were processed using the Microsoft Excel 2010 and IBM SPSS Statistics. The Mann-Whitney test was used to determine the reliability of differences. The data were plotted as error of arithmetic mean ( $\pm$ ). Pearson's  $\chi^2$  test was also used to analyse the trait prevalence within the groups. The Shapiro-Wilk's test for small samples was used to identify a normality of the distribution.

#### **Results and Discussion**

We examined an average vitamin D levels in the blood in different age groups of children (table 3).

	Age group					
	0-1	/ear	1-3 years		3-5 years	
Average value of	15,63±1,71		20,17±1,42		20,93±1,39	
Group I, n=50	n=20	40%	n=18	36%	n=12	24%
Average value of	40,79±3,105		40,12±2,16		43±2,45	
calcidiol, (ng/ml) Group II, n=25	n=10	40%	n=8	32%	n=7	28%

 Table 3 – Average vitamin D levels in the blood in different age groups

Table 3 shows that 40% of patients (n=20), children under 1 year of age in the main group had vitamin D deficiency ( $15.63\pm1.71$  ng/ml). In children aged 1-3 years, vitamin D level was ( $20.17\pm1.42$  ng/ml), and those aged 3-5 years (n=12) had  $20.93\pm1.39$  ng/ml. In the control group, vitamin D levels were within the normal limits.

We studied the vitamin D status in the breastfed and formula-fed infants considering the vitamin D fortification of infant formula.

In 60% of breastfed infants without a vitamin D supplementation, the average vitamin D blood level was 11.5 ng/ml, which is deficient (n=12). Sixty per cent of artificially fed children had a vitamin D value of 25 ng/ml (deficiency). However, this is not the normal level. A similar difference between the breastfed and formula-fed groups

was observed in the other age subgroups. The mean vitamin D blood levels in the breastfed and formula-fed children aged 1-3 years were 12.62 ng/ml and 22.49 ng/ml, respectively whereas in those of 3-5 years it was 14.9 ng/ml for the breast-fed and 23.30 ng/ml for the formula-fed patients. These data lead to the conclusion that the type of feeding among the surveyed children had an effect on vitamin D supply. The formula fed patients got a prophylactic dose with their formula, nevertheless there were also no children with normal blood levels of vitamin D, indicating the need for additional supplementation with cholecalciferol preparations.

A maternal morbidity was analysed to examine the factors influencing vitamin D availability in the children with respiratory pathology (figure 1).



Figure 1 – Chronic diseases of gastrointestinal tract/GIT in the patients' mothers

The mothers in the main group had a higher incidence of chronic gastrointestinal disease (40%). In the control group, only 8% of mothers were found to have the disease. We focused on the months of birth of children in the main and control groups in order to identify the dependence of vitamin D supply on the season of birth (table 4).

Month of birth	I group (main)		II group (control)	
	abs.	%	abs.	%
December	4	8	4	16
January	5	10	2	8
February	1	10	0	0
March	3	6	3	12
April	9	18	2	8
May	8	16	0	0
June	6	12	2	8
July	3	6	2	8
August	2	4	2	8
September	3	6	1	4
October	3	6	3	12
November	4	8	4	16

Table 4 – Months of birth of the children in the main and control groups

40% of children born in spring and 28% of those born in winter have low vitamin D levels. This might indicate the effect of the sunshine duration during the last trimester of pregnancy on the vitamin D status of a child. In other words, patients born in spring and winter are more likely to have low vitamin D levels.

The next stage of our research was to analyse the effect of sunlight on children's vitamin D supply.

The patients under study were permanent residents of Almaty. Information about the insolation in Almaty was taken from the official website [15,16]. According to these official data, the average duration of sunshine in Almaty is 2392 hours per year (99.7 days per year), which is higher than the same exponent in European countries.

The City of Almaty is known to be located at 43.2567 north latitude and 76.9286 east longitude, 787 metres above sea level, in a low insolation zone (fig.2).

The highest number of sunny days in Almaty is recorded in June, August and July. The least number of sunny days is recorded in February, January, March according to the data [17].



Figure 2 – The number of sunny days in Almaty

The city insolation importance is quite low given the low blood levels of vitamin D in the surveyed patients. Consequently, the main source of vitamin D is the dietary intake route.

The statistical accuracy of differences between the main and control groups was found by the U-Mann-Whitney test for independent samples, according to which the null hypothesis of equal categories of observation groups was rejected.

We see evidence of a high level of accuracy in the differences between the groups at p=0.05.

Table 5 shows the mean vitamin D levels in the main and control groups.

Surveyed group	abs.n	%	Mean vitamin D blood levels
Main group	50	66,67	18,54±0,97
Control group	25	33,33	41,43±1,56

 Table 5 – Mean vitamin D levels in the main and control groups.

The mean value of vitamin D in blood was fixed in the main group at a deficiency level of 18.54 ng/ ml, while in the control group it was 41.43 ng/ml. The ranking of vitamin D status in different nosological forms is shown in Table 6.

 Table 6 – Vitamin D levels in the children with different nosological forms

Diagnoses		Main group		
	under 10 ng/ml	10-20 ng/ml	20-30 ng/ml	over 30 ng/ml
Acute bronchitis	n=1(2%)	n=2(4%)	n=6 (12%)	n=11 (44%)
Acute obstructive bronchitis DN of 0-I stages	-	-	n=5 (10%)	n=6(12%)
Acute obstructive bronchitis DN of II-III stages	n=4 (8%)	n=4 (8%)	-	-
Acute bronchiolitis	-	n=1(2%)	-	-
Tracheitis	-	-	n=1(2%)	n=1(2%)
Unilateral focal pneumonia	n=3 (6%)	n=3 (6%)	n=6 (12%)	n=5 (10%)
Unilateral focal-drainage pneumonia	-	n=1(2%)	n=4 (8%)	-
Bilateral focal pneumonia	n=2 (4%)	n=2 (4%)	n=1(2%)	n=2(4%)
Bilateral focal-sprain pneumonia	-	n=1(2%)	n=1(2%)	-
Destructive pneumonia	n=1 (2%)	-	n=1 (2%)	-

The data in Table 6 indicate low vitamin D availability among patients with more severe nosological forms of respiratory pathology. Vitamin D levels after correction with cholecalciferol are shown in table 7.

|--|

	Before c	orrection	After correction		
Index 25(OH)D	abs.	%	abs.	%	
under 10 ng/ml	11	22	0	0	
10-20 ng/ml	13	26	3	6	
20-30 ng/ml	26	52	33	66	
over 30 ng/ml	0	0	14	28	
Total	50	100	50	100	

Table 7 shows the results between cholecalciferol and 25(OH)D gain after one month of vitamin D supplementation in 50 children in the main group. The baseline 25(OH)D level in the main group children was up to 10 ng/ml in 22% of children, 10-20 ng/ml in 26% of children and 20-30 ng/ ml in 52% of children.

In this group of children cholecalciferol was administered according to the following scheme: with 25(OH)D level less than 10 ng/ml - 4000 IU/day; 25(OH)D level 10-20 ng/ml - 3000 IU/day; 25(OH) D level 20-30 ng/ml - 2000 IU/day for a month. After the therapy, normal vitamin D levels were found in 28% of children, 66% showed an increase in 25(OH)D levels from 10-20 ng/ml to more than 20 ng/ml, and no patient had a deficiency.

It is obvious that this simple dosing scheme can make the task of correcting vitamin D deficiency in children much easier for public health practitioners.

## Conclusion

In a study of vitamin D status in children with respiratory pathology, 40% of children under 1 year of age in the main group showed a vitamin D deficiency of 15.63±1.71 ng/ml. A deficiency was observed in 40% of the breastfed children without additional vitamin D supplementation. One month therapy with cholecalciferol preparations was accompanied by normalization of vitamin D level in 28% of children, in 66% there was an increase in 25(OH)D level from 10-20 ng/ml to more than 20 ng/ml, and deficiency was not observed in any patient. Drug treatment of vitamin D deficiency and insufficiency will significantly reduce the incidence of hypovitaminosis and vitamin D-dependent conditions, as well as the frequency and severity of respiratory diseases in children.

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# RISK FACTORS ASSOCIATED WITH MORTALITY AMONG PATIENTS WITH COVID-19 IN ALMATY (KAZAKHSTAN)

SARS-CoV-2 caused by beta-coronavirus RNA spread from the Chinese city of Wuhan in December 2019 and it had been a global pandemic. Today, more than sixty-six million cases of infection are registered in the world, moreover above one and half million people die. For today's situation, 137 000 individuals are infected and approximately 2 000 people die in Kazakhstan.

To investigate the independent risk factors associated with Coronavirus-2 Severe Acute Respiratory Syndrome and mortality rate in Almaty (Kazakhstan).

A retrospective study was provided according to the participants' medical records with the COV-ID-19 and who were in the hospital in the period from June till August of 2020 in city hospital of Almaty, Kazakhstan. Among all 278 patients which were included to our issue 76 of them were unsurvived, and the rest were survived.

The survey has been conducted in a retrospective design of the medical records of those people with COVID-19 and patients who have been registered in Almaty city hospital, Kazakhstan in the period of June to August of 2020. Among all 278 participants who attached to our release, 76 of them were dead.

The correlation indirectly out of the seriousness of hepatocytes' cytolysis and the development in deceased patients severe type lymphopenia cause of the liver damage is a direct cytopathic effect on hepatocytes SARSCov2, since an absolute decrease in lymphocytes caused by virus-induced apoptosis correlated with the severity of viral load and is a significant and independent predictor of death.

**Key words:** Covid-19, causes, deaths, ARDS, pandemic, heart failure, multiple organ failure, risk factors, medical management, covid-19, postmortem medical records.

#### **Introduction. Background**

A very highly attention from the all over the world was attended to the Covid-19, which is known as a viral disease with the high level of contagiousness and which was firstly appeared in 2019 in a little Chinese city Wuhan. Behind time it was clear that the Covid-19's property of a big group of coronaviruses, then started to be well-known as SARS COV-2 [1,2]. After that the WHO called this illness as Covid 19. This disease is not restricted for a concrete location, so it has been distributed the planet without delay, and the cases which were happened due to this disease around the world. Many thousands of individuals from all over the world were died because of the Covid-19 and the risk's still remaining [3,4]. The influence of the Covid-19, together with the following quarantine, showed a very bad influence to the economy situation of the community, especially on production area, that will convey the impression for years [11-15].

#### Design, setting, and participants

In the period of quarantine (from June to August of 2020) [5,6] there was provided a retrospective research according to the participants' medical records with the COVID 19 and who were observed in the hospital in the city hospital of Almaty, Kazakhstan. Among all 278 patients which were included to our issue 76 of them were unsurvived, and the rest were survived.

The survey has been conducted in a retrospective design of the medical records of those people with COVID-19 and patients who have been registered in Almaty city hospital, Kazakhstan in the period of June to August of 2020. Among all 278 participants who attached to our release in the 2 stages. First was conducted with 188 survivide patients. Then 2-nd stage was providing with the 90 participants. Among the 278 participants the 76 of them were dead.

#### Results

To this research were attached a 278 of participants who were categorized into 2 groups related to such parameter as gender, that is revealed in the Table-1.

Table 1 - Gender categories

	Frequency	Percent	Valid Percent	Cumulative Percent
Male	78	41,5	41,5	
Female	168	58,5	58,5	41,5
Total	188	100,0	100,0	100,0

As it may be shown from the above graph, through the participants, who were attached to this issue, more than half of them were women with 58,5%. If we'll look to the numbers, it's clearly showed us that the incidence of the disease was more increased in female than in male.

The 8 categories of age groups were created for the participants attached in this issue (Table- 2).

According to the Table-2, the majority of patients were in the category of 50 to 59 years, followed by 60 to 69 years, which is 27,7% and 21,3%, respectively. Thus, the largest number of participants related to the age belongs to the age categories of 50 to 69 yrs. There is also a minimum number of patients under 20 years of age.

Age categories	Frequency	Percent	Valid Percent	Cumulative Percent
< 20	1	0,5	0,5	0,5
20-29	7	3,7	3,7	4,3
30-39	13	6,9	6,9	11,2
40-49	24	12,8	12,8	23,9
50-59	52	27,7	27,7	51,6
60-69	40	21,3	21,3	72,9
70-79	25	13,3	13,3	86,2
> 80	26	13,8	13,8	100,0
Total	188	100,0	100,0	

 Table 2 – Distribution of cases of diseases by age categories

In addition, the individuals from this research work based on racial origin were categorized by 4 groups. (Table-3)

As it can be clearly seen in Table number 3, those individuals who were attached in this issue were split up

into 4 ethnic categories: 1.Kazakhs, 2.Russians, 3.Koreans and 4.others. The results of this issue depicted us that in through the number of people who were participating in our research work were 66,9% Kazakhs, 19,3% Russians, 1,7% Koreans, and for others 12,2%.

 Table 3 – Nationality parameters of participants

	Frequency	Percent	Valid Percent	Cumulative Percent
Kazakh	121	66,9	66,9	66,9
Russian	35	19,3	19,3	86,2
Korean	3	1,7	1,7	87,8
Others	22	12,2	12,2	100,0
Total	181	100,0	100,0	

The individuals, who were taken to our issue have been split up in seven groups by their parameters of social status in the Table 4.

As can be shown from Table 4, the majority of patients with 42,3% leads to the group of unem-

ployed. Further, retired category of patients has been considered for a big amount with 29,7% of respondents. Contrastingly, in the disabled group, the smallest number of patients was received -2(1.8%).

Table 4 – Social status of patients under study

	Frequency	Percent	Valid Percent	Cumulative Percent
Employed	17	15,3	15,3	15,3
Unemployed	47	42,3	42,3	57,7
Housewife	11	9,9	9,9	67,6
Retired	33	29,7	29,7	97,3
Disabled	2	1,8	1,8	99,1
Other	1	,9	,9	100,0
Total	111	100,0	100,0	

High mortality rates of individuals were linked with the cause of late hospitalization, not appropriate doses of corticosteroids, very low amount of time for laboratory and instrumental assessments, insufficiency of medications in the hospital and additionally indecorous duration of treatment, which are shown in Figures 1-2.

As can be seen in (Figures -1 and 2), 38.6 per cents of those patients who were died in pandemic

time were hospitalized late in extra hard and serious condition. Patients with late hospitalization had a high mortality rate -93%. Not correct dose of glucocorticosteroids, lack of laboratory and instrumental studies, not appropriate amount of medications in the hospital and not timely therapy initiation were difined as the remain causes of mortality.



Figure 2 – Mortality rate in different patient groups

The figure number 2 depicts us, that 20% of individuals didn't take an enough doses of drugs within corticosteroids which could have been make better conditions. By the recommendation of WHO [4], the usage of glucocorticosteroids can deteriorate the mortality rate in those one, who are standing in extremely hard condition adding with no ventilation indicating, except for patients with total contraindications of steroid therapy to 7-10 days.

The above figure shows that 20% of patients did not receive enough medications, including GCS, to improve their condition. According to the Who recommendation [4,10], the use of corticosteroids leads to a decrease in mortality in patients with severe conditions and lack of indications for lung ventilation, with the exception of patients with absolute contraindications to 7-10 days of steroid therapy.



Figure 3 – Lack of drugs and initiation appropriate therapy

The patients were in critical and very serious condition. By this case, the intensive care unit was full and the medication was finished. Accordingly, approximately 13,3% of patients were unable to appoint corticosteroids because of the high patient attendance and high need for corticosteroids.



Figure 4 – Lack of opportunity to conduct laboratory and instrumental research

Consequently all hospitals with their intensive care units were filled with seriously ill and extremely serious ill individuals. Not enough resources for medical care providing to patients were observed.

The findings of our study has been presented, as it's shown in Figure 5, the majority of mortality of individuals in case of Covid-19 were firstly from ARDS, secondly from multi-organ failure, pulmonary embolism, and from heart failure.

As it can be clearly seen in the figure-6, the majority cases of the disease in the category of ages 50 to 69 with 27,7% and 40 21,3%, consequently. Thus, the very increased amount of individuals according to the ages is conducted for 50 to 69. In terms of the lowest amount of individuals the group under 20 years.

Additionally, according to the mortality causes, like: ARDS, heart failure, pulmonary embolism and multiple organ failure, survivors were divided by ages of groups.

In consonance with the distribution of causes of death by age group it was given the results such as most of people in the groups of ages "75 to 79" and "55 to 59" were the dominant one, where the cause of mortality was ARDS, 14.29% and 14,28%, respectively. What's for group of individuals with HF, the most of patients' (33,33%) death went to the age's category of 55-59 years. Another died from multiple organ failure, with the highest percentage (16,67%) - aged 50 to 54 years.



Figure 5 - Causes of unsurvived among deceased according gender



Figure 6 – The mortality structure of causes in dead patients according to the age

### Conclusion

Thus, indicators such as gender, age and nationality are the most important risk factors for mortality in people with Covid-19. Virtually all countries affected by the disease, including Kazakhstan, have developed mitigation and containment strategies based on social distancing.

In Kazakhstan, the pandemic fell in the summer, which is more likely due to the end of strictly quarantine, non-compliance with quarantine measures in public places and mass movement of people around the country [7,8,9]. As a result, hospitals were extremely overcrowded with patients from moderate to serious condition. Patients were admitted in serious condition, daily mortality increased, the intensive care unit was overcrowded, and there was an acute shortage of instruments and drugs for patient care. This analysis showed that coronavirus infection requires strict compliance of people, the need to enlarge the amount of multidisciplinary medical personnel, and improve the equipment of hospitals with all the necessary drugs and instruments.

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# Section 2 Clinical case

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# PERFORATION OF THE RIGHT ATRIUM WITH THE DEVELOPMENT OF RIGHT-SIDED PNEUMOTHORAX AND PNEUMOPERICARDIUM IN A PATIENT WITH AN IMPLANTED DUAL-CHAMBER PACEMAKER

Development of pneumothorax after pacemaker implantation is an uncommon complication. Pneumothorax, contralateral to venous access site, due to atrial lead perforation is a more rare complication. The most frequently reported predictors of lead perforation are active fixation leads, low body mass index, older age, female gender and concomitant anticoagulation therapy.

We described a clinical case of a 69-year-old patient who had undergone radiofrequency ablation of atrial fibrillation several years earlier. Several years later, the patient developed sick sinus syndrome (chronotropic incompetence) and bifascicular block, as a result of which he was implanted with a dual-chamber pacemaker, which was subsequently complicated by perforation of the right atrial appendage with damage to the middle lobe of the right lung with the development of pneumothorax and pneumopericardium. Described cases illustrates that if right pneumothorax symptoms occur in a patient where the device was placed from a left subclavian approach, perforation of the atrial appendage should be excluded. By far the preferred method of diagnosing this complication today is chest CT scan.

**Key words:** perforation of the appendage of the right atrium, pneumopericardium, right-sided pneumothorax.

# Introduction

Development of pneumothorax after pacemaker implantation is an uncommon complication and occurs in 1% of pacemaker implantations [1, 2].

Contralateral to implantation site pneumothorax is an infrequent complication [3].

We present a case of concomitant right-sided pneumothorax and pneumopericardium following left-sided pacemaker implantation due to atrial lead perforation 12 hours after procedure.

## **Case report**

A-69-year-old man presented with recurrent episodes of palpitations for six months. There was

no history of syncope. The electrocardiogram and Holter monitoring shown bifascicular block, intermittent chronotropic incompetence. The dual chamber pacemaker implantation was performed using left subclavian venous access. A right atrial lead (active fixation) was positioned in the RA appendage, and right ventricular lead (active fixation) was positioned at the interventricular septum. Leads sensing, pacing threshold, and impedance were within the expected normal ranges (RA lead: pacing threshold -0.6 V/0.4 ms; sensing -3.9 mV; impedance -520 $\Omega$ ; RV lead: pacing threshold – 0.5 V/0.4 ms; sensing -8 mV; impedance  $-750 \Omega$ ). The chest radiographic examination performed after the procedure did not reveal any abnormalities, suitable lead position and no signs of pneumothorax.



Figure 1 – Chest radiographs (left) and CT scan (right) in the anteroposterior views illustrate right atrial lead in the anterolateral position of the right atrium appendage and the right ventricular lead in the interventricular septum. There were no signs of pneumothorax or hemothorax.

Approximately 12 hours later, the patient complained of sudden onset of shortness of breath. His vital signs at that time were blood pressure 130/80 mm Hg, heart rate 60 bpm, respiratory rate 18/min, and oxygen saturation 98%. Device interrogation demonstrated changes in the RA lead parameters (right atrial pacing was ineffective – pacing threshold more than 7 V/0.4 ms; sensing threshold, 0.7 mV; lead impedance, 410  $\Omega$ ). Chest radiography showed right-sided pneumothorax and normal leads position. Drainage of the right pleural cavity was performed with the installation of the right intercostal drainage until the signs of pneumothorax disappeared. CT-scan showed a small right-sided pneumothorax with perforation of the right atrium appendage, right pleural cavity and right lung with the development of mild pneumopericardium.



Figure 2 – Chest CT scan image 1 day after pacemaker implantation. A) and B) Axial CT image shows the right-sided pneumothorax, right atrial appendage perforation by atrial lead, and pneumopericardium. C) Coronal CT image showing the atrial lead perforation through the right atrial appendage, pneumopericardium.

Taking into account the dislocation of the right atrial lead into the right pleural cavity, with perforation of the appendage of the right atrium, right lung, and the lack of adequate right atrial stimulation, we decided to perform a right-sided minithoracotomy with suturing of the right atrial defect, and reimplantation of the RA lead using a endocardial electrode with passive fixation.

In the left subclavian region, an incision was made along the previous suture, and the subcutaneous tissue was dissected. The pacemaker was pulled out and the right atrial electrode was disconnected. An introducer was introduced through the electrode into the lumen of the left subclavian vein for explantation of the previous one and further implantation of a new endocardial electrode of the right atrium with passive fixation. After that, a right-sided minithoracotomy was performed. When examining the pleural cavity, 2 centimeters of the distal tip of the endocardial electrode with damage to the pericardial cavity and pleural cavity are visualized.



Figure 3 – Perforation of the right atrium, pericardium, right pleural cavity with the right atrial lead.



Figure 4 – Damage site of the middle lobe of the right lung.

There was an insignificant volume of blood in the pleural cavity. After pericardiotomy, the site of perforation was verified – it was the apex of the right atrial appendage. No liquid blood was found in the pericardial cavity. A purse-string suture was applied around the electrode, after which the electrode was inserted into the cavity of the right atrium, additional sutures were applied to the wound area.



Figure 5 – Sutured site of damage to the right atrial appendage.

After thorough hemostasis and suturing with single sutures of the pericardium with the installation of a drainage tube into the right pleural cavity, the chest was closed. Immediately after that, the second stage was performed explanation of the previous (active fixation) and implantation of a new (passive fixation) RA-lead. The patient recovered without complications. The patient was discharged 3 days later with an appointment for a planned outpatient visit 3 weeks after surgery.

#### Discussion

Complications associated with pacemaker implantation occur in a variable percentage of

cases, ranging from 3.2% to 7.5% [4, 5]. Pneumothorax is typical complication of subclavian venous access [2]. Contralateral pneumothorax and pneumopericardium is a rare complication after pacemaker implantation and may not be reveal on chest radiography and device testing [6, 7, 8]. Several risk factors may be responsible for the increased complication rate such as an extremely thin-walled atrial appendage, stiffness of the atrial lead helix, over-screwing, and the experience of the operator.

To the best of our knowledge, only some few cases have been described, the details of which have been summarized in **Table 1**.

Table 1 - M - Male; F - Female; AV - Atrioventricular; A/L - Anterolateral; RA - right atrium.

Authors	Age/	Diagnosis	Atrial lead	Symptoms/	Chest X Ray	Change	Treatment
	sex		(Site of	signs		In	
			implantation,			lead	
			Position, Type)			param.	
Sebastian	73	Mobitz	Left subclavian,	Sudden chest	50% pneumothorax.	No	Intercostal drainage
et al.	(M)	type II AV	A/L RA;	pain;	Pneumopericardium		tube
		block	Active fixation	2 days.			

Perforation of the right atrium with the development of right-sided pneumothorax and pneumopericardium ...

Srivathsan et al	77 (F)	Sick sinus	Left subclavian, $A/L RA$ .	Shortness of breath	30% pneumothorax.	No	Intercostal drainage
	(1)	<i>by ind c int</i>	Active fixation	8 hours.	(Moderate sized)		extraction
Nantsupawat	83	Tachy-	Left subclavian,	Chest pain,	10% pneumothorax.	No	Observ,
et al.	(M)	brady syndrome	A/L RA; Active fixation	neck pain; 1 day.	Pneumopericardium (Small sized)		oxygen inhalation
Parashar et al.	62 (M)	Mobitz type II AV block	Left subclavian, A/L RA; Active fixation	Chest pain; 7 hours.	50% pneumothorax. Pneumopericardium (Small sized)	No	Intercostal drainage tube
Chryssagis et al.	65 (F)	Unknown	Right subclavian, A/L, in the middle of RA; Active fixation	Chest pain, Shortness of breath, Hypotension; 1 week	Pleural and pericardial effusions	Yes	Median sternotomy
Present case	69 (M)	Bi- fascicular block	Left subclavian A/L RA; Active fixation	Shortness of breath, chest pain; 12 hours.	30% pneumothorax. Pneumopericardium (Small sized)	Yes	Intercostal drainage tube, Minithoracotomy

Patients with contralateral pneumothorax commonly present with chest pain and/or shortness of breath. In published in Table reports, symptoms typically occurred within 1–7 days after device implantation.

Attention is drawn to pneumopericardium revealed by CT data in almost all cases was described, but there is no sings of the presence of fluid in the pericardium. This is most likely due to the fact that the atrial lead itself may have plugged the defect.

The most frequently reported predictors of lead perforation are active fixation leads, low body mass index, older age, female gender and concomitant anticoagulation therapy [9]. In our opinion, the cause of perforation in our case may be a combination of excessive screwing of the atrial lead helix during placement and the presence of a thin atrial wall.

According to published data of CT scan, cardiac perforation occurs in about 0.3% of all implantations of pacing devices, of which approximately 15% of atrial perforations and 6% of ventricular perforations are asymptomatic [10,11]. According autopsy study myocardial perforation or penetration by an electrode was recognized in 5.3% cases of patients 60 years of age or over with an implanted pacemaker. The perforation rate was 27.3% in active-fixation atrial leads, and 0% in 10 passive leads [12].

CT scan allowed to verify complications in all cases of contralateral pneumothorax, pneumopericardium, and/or lead perforation after device implant [13, 14, 15].

Therefore, it is obvious that computed tomography of the chest is the diagnostic method of choice when there is clinical concern of cardiac lead perforation. As for the treatment, the insertion of intercostal tube should be considered when pneumothorax includes more than 10% of pleural space [6, 7, 8]. With unchanged parameters on the atrial lead during interrogation, and the absence of clinical symptoms of perforation, electrode repositioning most authors was not considered.

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# Conclusion

Contralateral pneumothorax with or without pneumopericardium is an infrequent complication and may not be verified on chest radiography and device interrogation. Awareness about the possibility of this complication is important. An augmented degree of attention should exist for all physicians dealing with similar patients.

If a right pneumothorax develops in a patient where the pacemaker was positioned from a left subclavian approach, perforation of the right atrium should be considered and immediately investigated. By far the preferred method of diagnosing this complication today is chest CT scan.

Treatment, in turn, depends on symptoms, hemodynamic status, size of pneumothorax, and device parameters.

Conservative management without the use of a drain tube or atrial lead extraction may be sufficient in patients with stable vital signs, stable lead parameters, and mild pneumothorax and pneumopericardium.

Remember to use caution when screwing the atrial lead during insertion in patients with enlarged and most likely thinned atrial walls.

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# REACTIVATION OF BRUCELLOSIS AND RHEUMATOID ARTHRITIS IN PREGNANCY

Brucellosis is a zoonotic infectious-allergic disease caused by bacteria of the genus Brucella, mainly characterized by damage of the musculoskeletal, nervous, genitourinary, and other organ and systems. In women, brucellosis results in miscarriage, primary or secondary infertility. But little is known about the course of pregnancy with a combination of brucellosis and autoimmune pathology such as rheumatoid arthritis.

Report the course and outcome of brucellosis and rheumatoid arthritis in pregnancy

We analyzed a clinical case of a pregnant woman with chronic brucellosis and rheumatoid arthritis. In a patient with chronic brucellosis in the first trimester of pregnancy, brucellosis intensified with

the development of acute monoarthritis. Arthritis regressed after a course of antibiotic therapy in the second trimester, but there was an activation of rheumatoid arthritis and preterm labor in the third trimester.

This case showed a more severe course of brucellosis during pregnancy compared with rheumatoid arthritis and the importance of antibiotic therapy to prevent severe complications.

Key words: Brucella, Brucellosis, Rheumatoid Arthritis, Pregnancy, Zoonotic Infection.

## Introduction

Brucellosis is a zoonotic infection transmitted to humans through unpasteurized meat and dairy products of infected animals or by direct contact with the pathogen through the mucosa, respiratory tract, or damaged skin [1]. This disease, which infects more than 500,000 people annually, can affect any organ, cause disability, and thus becomes a socially significant pathology in the world [2]. In Kazakhstan, the incidence per 100 thousand of the population decreased from 13.2 (2010) to 6.1 (2018), but despite a significant decrease in the incidence, brucellosis remains among the most dangerous infections [3]. There are 12 species of Brucella, of which 4 are pathogenic for humans: Brucella melitensis, Brucella suis, Brucella canis and Brucella abortus, the latter of which is more common in Kazakhstan [4]. Brucellosis affects any organ where it metastasizes, and in particular Brucella abortus causes pelvic inflammation with consequences for miscarriages, primary or secondary infertility and premature birth. Treatment for brucellosis is to eradicate the pathogen and boost the immune system. On the other hand, rheumatoid arthritis (RA) is an autoimmune pathology, the treatment of which is aimed at reducing immunity. RA often affects women of fertile age, causes arthritis in the small joints of the hands,

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and leads to early disability [5]. Pregnancy aggravates the course of both brucellosis and RA. In this case report, we described the course and outcome of the disease in a pregnant woman with chronic brucellosis and rheumatoid arthritis [6,7].

## **Case presentation**

A 38-year-old pregnant woman, mother of 4 healthy child, had sevenths pregnancy with twins. In the 13th gestational week she complained of edema, pain and limitation of movement in the right knee joint, crepitus in large and small joints of the body, general weakness and rapid fatigue. Since childhood, her family has kept cattle, there have been miscarriages in cattle and small ruminants. She was infected with brucellosis at age 24-year-old though direct contact with infected meat and milk. At the age of 33, she was diagnosed with rheumatoid arthritis with lesions of the small joints of the hands and positive anti-CCP, rheumatoid factor (RF). The patient received methotrexate at a dose of 15 mg/ week and GCS 16mg/day before pregnancy. progesterone At 13 weeks, the patient received azithromycin 1000mg / day for 42 days and progesterone. From 20 weeks, the patient had an increase in morning stiffness and pain in the hands. At 34 weeks, she developed preeclampsia with increased blood pressure and proteinuria. Life history: a single miscarriage up to 12 weeks. Objectively: acute arthritis of right knee joint. Laboratory tests revealed a positive brucellosis test, a positive ACCP, an inflammatory blood reaction that increased in the third trimester and anemia (table 1). At 34 weeks of gestation, the patient developed preeclampsia, pain and inflammation of the small joints of the upper extremities, therefore, she was treated with a calcium antagonist 10 mg / day, aspirin 50 mg / day, and methylprednisolone 8 mg. At 35 weeks premature birth occurred with the birth of a slink boy and girl. To date, the patient breastfed and is taking GCS 8 mg/day, hydroxychloroquine 200 mg/day.

Timing	13 weeks	34 weeks	Normal values	
ALT (U/I)	15.2	47	(0–45mmol/L)	
AST (U/I)	16.7	46	(0-42mmol/L)	
Total bilirubin		17	(5.1–19.0 μmol/L)	
Direct bilirubin		2	(1.7-6.8 µmol/L)	
Glucose (mmol/L)		4	(3.89 – 5.83 mmol/L)	
ESR (mm/h)	27	38	(<15 mm/h)	
Leukocytes	7.7	10.8	$(4-9 \text{ x} 10^9/\text{L})$	
Lymphocytes	32	28	(18-42%)	
Platelets	226	387	(180-320 x10 <sup>9</sup> /L)	
Erythrocytes	4.9	3.5	$(3.7-4.5 \text{ x}10^{12}/\text{L})$	
Hemoglobin	129	77	(120-140g/L)	
ELISA Brucellosis	IgG positive		(Negative)	
ELISA anti-CCP	701	484.7	(0-17 U/mL)	
Protein in urine	0.33	0.330	(0-0.033g/L)	
Leukocytes in urine	1-2	22	(3-5)	

#### Table 1 – Laboratory results

ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, ESR: Erythrocyte sedimentation rate, anti-CCP: Anti-cyclic citrullinated peptide

### Discussion

Various sources provide data where brucellosis ends in full-term delivery [8,9,10], but also describes cases of spontaneous abortion and premature birth [11,12,13]. We presented a case of chronic brucellosis activation in a pregnant woman with rheumatoid arthritis. She contracted brucellosis at age 24. In the first trimester of the 4th pregnancy at the age of 38 years, the patient developed symptoms of active brucellosis: monoarthritis of the right knee joint. She was treated with azithromycin 1000mg per day for 42 days. In the first two weeks of antibiotic therapy, there was an increase in pain, swelling and movement in the joint with subsequent regression of arthritis. Pain in the small joints of the hands began to bother the patient in the second and third trimesters. Despite the fact that rheumatoid arthritis intensifies and aggravates pregnancy, our case showed that zoonotic infection is more dangerous, causing the risk of miscarriage or premature birth [14,15]. Thus, the treatment of brucellosis during pregnancy is a priority in comparison with rheumatoid arthritis, as it leads to miscarriages, intrauterine fetal death or premature birth.

#### Conclusion

1. Chronic brucellosis intensified in early pregnancy and regressed after a course of antibacterial therapy.

2. Rheumatoid arthritis manifested in late pregnancy

3. Despite the antibacterial and anti-inflammatory therapy, labor was premature at 35 weeks.

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# Section 3 Review article

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# THE «TEACHING – RESEARCH» NEXUS IN MEDICAL EDUCATION

Research forms an important part of the academic competencies attained during academic study. For medical students, this includes learning how to critically appraise and interpret medical and wider health care research, particularly – but not only – when relevant for one»s own current or future practice. It also includes understanding the core principles of different methods and research ethics and learning to participate in research. The teaching – research nexus: strategies to implement research education in the medical curriculum. In this paper, we offer reflections on how to do this on the basis of professional anecdotal experiences by a general educationalist with a particular interest in medical education; an undergraduate medical student with a research-focussed, stand-alone additional degree, and a medical academic.

Our paper initially explores the need for research education; tying in Healey»s theoretical framework in student research, and the nature of providing evidence-based patient care. The paper then presents a report on a student research programme at the University of Birmingham, England.

Key words: tteaching, research, medical education.

## Introduction

«Research» as a competency for medical doctors.

There are numerous national and international competency frameworks guiding both medical practice and medical education. Research competencies form an important part of the standard competencies described in these frameworks. An example of this includes the Canadian «CanMEDS 2015 Physician Competency Framework» [1], which defines the abilities physicians require to meet the healthcare needs of the people they serve. These abilities are grouped thematically under seven roles: the Medical Expert (an integrating, overarching role), Communicator, Collaborator, Leader, Health Advocate, Scholar and Professional. The role of the Scholar encompasses competencies concerning interpreting and conducting research, with a strong focus on «Evidence Based Medicine».

Universities globally have adapted these professional competency frameworks to their medical curricula. In these curricula, professional competencies are usually «translated» into student learning outcomes.

The «Subject Benchmark Statement Medicine», published by «The Quality Assurance Agency for Higher Education» [2] may be considered as a British educational translation of a medical competency framework. When addressing student-selected study, the statement states that this should aim to «stimulate critical thought» and «develop further generic graduate skills and intellectual attributes underpinning enquiry and critical thinking». Additionally, this should enable students to «acquire research methods and enhance their skills in collection, evaluation, synthesis and presentation of evidence».

In Britain, the «General Medical Council» publishes the «Generic professional capabilities framework». It states: «This framework sets out the essential generic capabilities needed for safe, effective and high-quality medical care in the UK. At its heart are the principles and professional responsibilities of doctors, and we have translated these into educational outcomes so they can be incorporated into curricula» (our italics.) The framework of the document shows a strong resemblance with the CanMEDS framework. Educational outcomes are grouped in nine domains. Domain 9: «Capabilities in research and scholarship» states that «Doctors in training must demonstrate that they can:» Followed by 12 research related learning outcomes, including «demonstrate appropriate knowledge of research methods, including qualitative and quantitative approaches in scientific enquiry.» [3].

An example of a direct «translation» of the Can-MEDS framework is the 2009 framework for undergraduate medical education in the Netherlands [4], in which the seven roles of the CanMEDS framework are explicitly retained, alongside a strong focus on the importance of research education. It states that «Student-selected study has the aim of stimulating critical thought and developing further generic graduate skills and intellectual attributes underpinning enquiry and critical thinking; it should allow students to acquire research methods and enhance their skills in collection, evaluation, synthesis and presentation of evidence».

The teaching – research nexus: strategies to implement research education in the medical curriculum.

The strategies medical schools employ globally to enable students to acquire research competencies are varied: ranging from optional, additional teaching in addition to core curriculums, to a mandatory, significant portion of undergraduate education. As an example, Maastricht University medical school in the Netherlands employs Problem Based Learning from the first day of their undergraduate degree course. Its principles and practice are explained in an excellent short cartoon style video [5]. In the video a student says: «with PBL we learn more than just facts» and: «we learn to conduct our own research», showing inspiration and enthusiasm.

The clinical context: Combining professional competencies in practice. PBL is not the only possible approach to research education in medical studies. A medical doctor must combine their professional competencies constantly in daily practice. The care for patients is central, not the separate medical knowledge and skills that are reflected in subject areas like anatomy, immunology, physiology, etc. and also research skills. CanMED: «As Medical Experts, physicians integrate all of the CanMEDS Roles, applying medical knowledge, clinical skills, and professional values in their provision of high-quality and safe patient-centred care». So, the integration of these competencies in medical education bachelor and master programs also should receive due attention. Often this integration was – and still is – confined to the final year of the programme in a series of clinical attachments in different medical specialties. However, the earlier in the curriculum this integration is pursued, like in PBL, the closer the educational development of students will be linked to their later professional practice.

So, research competencies should be part of this integration. In the remainder of this article we will concentrate on how these specific research competencies can be integrated in a medical curriculum.

*How can the teaching – research nexus be implemented in daily educational practice?* 

There are many educational research papers published about the teaching – research nexus. For instance, using «teacher – research nexus in medical education» as a search term in Google Scholar gives an overwhelming number of hits. However, most of these publications do not provide accessible, practical and succinct support to medical teachers who are often, next to their teaching load, very busy with clinical and/or research work.

Professional development workshops can provide teachers with teaching – research models and examples in an effective way, especially when collegial exchange is a cornerstone of the workshop approach [6]. Also «teacher guides» and frameworks can provide (medical) teachers with practical support.

A first example of such a guide is published by the University of Portsmouth in Britain and Nagoya University in Japan and covers «Eight principles for linking research and teaching» [7]. These principles summarize what can be done in classroom practice. The guide states that teachers could (or should):

1. Communicate the excitement of doing research.

2. Draw on your own research experiences.

3. Emphasize the process of knowledge production.

4. Include current research findings and issues in your teaching.

5. Provide opportunities to acquire research methods and skills.

6. Involve students in various research activities in your institution.

7. Create showcases of undergraduate research.

8. Introduce students to the lives and values of researchers.

Each of these eight principles is subdivided in a number of practical tips. For example, the first

principle «Communicate the excitement of doing research» provides the following:

A. Talk about your motivation for doing research.B. Communicate the enjoyment of doing re-

search in your field. C. Share the excitement of producing knowledge.

D. Explain why research skills are important for students.

E. Explain how research outcomes make a difference to students» daily lives.

F. Engage students through interesting demonstrations and examples.

Finally, each principle is linked to one or a few practical examples on research skills training from Portsmouth or Nagoya University. For instance, for the principle «Emphasise the process of knowledge production» it is described how diffraction is taught in a course on crystallography. Students do a very open experiment with diffraction patterns of light falling through pieces of cloth and learn to reason in a scientific way to explain what they see.

The second example is a framework on student research that was originally developed by the University of Adelaide in Australia. «The Research Skill Development (RSD) framework was devised in 2006 to articulate what educators do when they facilitate student learning through active exploration in ways that enable their skills to grow in sophistication and rigour». Since 2006 the RSD has been adapted and re-published by many scholars and educational practitioners. Please be advised to click the link below to the framework, to support the following brief explanation.

On the y-axis of the framework six consecutive research skills are described. On the x-axis there are seven divisions on student research, ranging from «predescribed research», which is very closed and supervisor instigated, to «enlarging research», in which students act as «fully fledged» independent researchers. Each resulting square has a concrete description of the development of a particular skill at a particular level. The framework can be used to design a research curriculum or to analyse an existing one. It can also be used as a rubric [8] to assess the student learning process by attainment levels.

In 2015 the journal «Nature» published the article «The Science of Teaching Science» [9]. In this article, an approach to learning about research is advocated that is based on active student participation, at bachelor and master level, in the sciences, and in medicine. The article starts with a medical example: the description of a first-year medical student group task to help «solve» the cause(s) of an outbreak of food poisoning among a number of people attending a particular event. The article describes many other examples of effective educational methods of active learning and concludes: «what the methods share is an outcome confirmed in hundreds of empirical studies: students gain a much deeper understanding of science when they actively grapple with questions than when they passively listen to answers».

### Mick Healey»s framework of research training

Together with several colleagues, Mick Healey of the University of Gloucestershire in Britain has published widely about the teaching – research nexus. His publications are also quoted extensively in the educational literature about this nexus and includes research work and guidelines for teachers, departments and institutions [10-11].

The core of his approach is the «teaching – research framework», in which four types of student research can be distinguished [12]. This framework helps to understand, classify and balance the many different approaches that exist in student research training.



#### STUDENTS ARE PARTICIPANTS

Figure 1 – Mick Healey»s framework of research training

The framework has two axes. The X-axis is a continuum between emphasis on research content» to emphasis on research processes and problems. The Y-axis ranges from students as audience to students as participants. This leads to four different approaches to student research education. Student research education can be:

Research-led: where students learn about research findings, curriculum content is dominated by staff or current disciplinary research interests, and some or much of the teaching may emphasise information transmission.

An example pertaining to an endocrinology or virology course: in a lecture student are taught about the medical implications of a covid infection, using a current scientific article as the basis for the lecture.

Research-tutored: where students learn in small group discussions with a teacher about research findings.

Students compare and discuss two recent medical articles with diverging viewpoints about the transmission vectors of the covid-19 virus.

Research-oriented: where students learn about research processes, the curriculum emphasises as much the processes by which knowledge is produced as knowledge that has been achieved, and staff try to engender a research ethos through their teaching.

In a series of lectures and practicals students study different research articles from the methodology point of view: their set up, the format, the type of research (qualitative – quantitative), the statistics utilized, the ethical implications, etc. Furthermore, students train with the formulation of research questions, hypotheses, selecting appropriate research methods, etc.

Research-based: where students learn as researchers, the curriculum is largely designed around inquiry-based activities, and the division of roles between teacher and student is minimised.

For example, students do a complete research project, from the formulation of a research question up to the publication of the results. The lecturer acts as a research coach, helping where necessary but leaving the ownership of the research very much with the students (see below for an extended example from the medical school of the University of Birmingham.)

## Some remarks about Healey's framework

Healey emphasises that all four forms of research education have their own value. In education practice, there is no preference for one of them, nor a preferred sequence in time. In a balanced medical curriculum, all four forms will have their place! Each of the four forms of research education can be realised in many different ways and at all levels of (medical) education. Unfortunately, it is still a common misconception that «research-based learning», where students are in charge of the whole research process, only can take place at the end of a bachelor or even master program, after they have «mastered» all research tools and techniques necessary for «proper» research. In the medical educational literature there are many examples that medical students can engage in full research even from the beginning of their first year.

An example of «research-based learning in the first year of medical education is given by Prof. Friedo Dekker of the Medical Center of Leiden University in the Netherlands [13]. He (quote) «asked all 1st year Bachelor of Medicine students to do a 2-week clinical attachment in a nursing home in September, to collect data on 3 selected patients (comorbidities, laboratory results, medication, ADL, cognition), to create a SPSS database, to go back to the nursing home in December, to collect same data (on same patients they collected data from in September?), to formulate a research question, to participate in a course with 5 days of lectures, assignments, practical and small working group sessions, to present a research question, to present a research project, and to write a short report.» Of course, this type of student research does not necessarily lead to publications in peer reviewed medical journals. It is often published in «student research journals» and/ or presented at student research conferences.

Individual teachers can use the framework to assess their own teaching practice. Which forms of research education are part of my repertoire? How could I engage in different forms of research education? Is my research teaching «implicit» or do I make my students aware of its research components? How do I use my own research as part of my teaching? Etc.

The framework also can be very useful at the level of a department or institution. A curriculum evaluation analysis can be performed on the basis of the framework to find out which forms of implicit and explicit research education take place across the different disciplines of the curriculum, how they overlap or interfere and which omissions come to the fore.

Finally, the framework can also be an important cornerstone in medical curriculum design.

A case study: the BMedSc programme course «Global Health» of Birmingham University, UK. The University of Birmingham (UK) offers a research-oriented Intercalated BMedSc Degree Course Global Health, where medical students take 10 months out of their standard programme after their 3rd or 4th year of study [14]. This program is for those students who wish to explore global health as potential future health professionals and/or academics, carry out original field research or literature study, share the results of their work with host communities and get their research published.

During their research year, students engage in a number of different activities, covering all four quadrants of the Healey framework, with an emphasis on research oriented and research-based approaches. Students receive a firm grounding in health policy, social determinants of health, communicable and non-communicable disease control, and rigorous qualitative and quantitative research methods. Furthermore, research ethics are taught as well as challenges in research of pharmaceuticals, medical appliances and large health/ health care data source, the direction of RD, Intellectual property rights and global social justice. Principles of advocacy, innovation and fundraising are also taught. There is a strong focus on experiential learning, where students, through their group work, presentations and debates, «own» and create, rather than receive their learning. Overseas field studies are typically carried out in collaboration with clinicians/academics/students in the host country over an 8-12-week period early in the calendar year. Ethical approval processes are rigorous and in full compliance with the hosts» requirements.

Research topics are often proposed by health professionals in overseas settings and include a variety of topic such as:

Qualitative research on perceptions around obstacles to trachoma control in West Africa.

Perceptions of men of their health care seeking behaviour in East Africa.

Vectors of Chagas disease in Bolivia.

Quantifying the need for surgical and anaesthetic training in Sierra Leone.

Knowledge and attitudes around postnatal depression in a hospital setting in SE Asia.

Access to health care and perceptions of women admitted to hospital for miscarriage in Southern Africa.

And more...

Research can be one-off, or year-on year, adding further value by building on previous studies, as in the Loreto region in Peru, where our students respond to local health research priorities. Results are fed back to the health services in the host setting.

During 2020-21, due to corona restrictions, studies by remote interviewing were carried out,

mainly in the UK. The main focus was on perceptions of corona control responses by selected groups in different countries, with the aim of learning from each other»s experiences and informing the development of better preparedness for future, unknown, large-scale and severe global health and health care challenges at local, national and global levels.

While prior academic achievements may be predictive of success, students are warned that this is not always the case for this programme, which is «outside the box» of customary medical education.

A large proportion of studies is published in mostly open access peer reviewed academic journals. For example, see references [15,16,17]. Please note that almost all first authors are the students, who were the «Principal Investigators». Apart from fulfilling the duty of making research findings easily available to researchers, practitioners and populations, it adds to the student»s credentials as an accomplished researcher in their CV.

While student satisfaction during and immediately after the course was generally high, a weakness of the programme is that it does not yet have a system to capture feedback from alumni who now practice medicine.

Student perceptions of research training.

During their studies, students take many different courses. Some students find some courses less inspiring, other students find the same or other courses inspirational or even «life changing», as is anecdotally the case for students in the above case study from Birmingham University. In addition to the question of what students feel about a course it is also important to ask what they learn from it. It is safe to assume (and research shows) that students learn more from courses that employ active learning methods, during which students feel intellectually and emotionally engaged, than from courses based solely on book knowledge and rote learning.

To appraise and improve the quality of research education it is important to evaluate the learning outcomes of the students. That can be done by grading tests, assessing practical skills, benchmarking student research papers, etc. An important aspect of such evaluations is to determine the perceptions students have regarding their learning processes & learning outcomes and their perceived development towards professional medical practitioners.

An example of this type of educational research is reported in the publication What Do Medical Students Understand by Research and Research Skills? Identifying Research Opportunities Within Undergraduate Projects [18]. A mixed methods approach was used to answer this question for five medical schools in the UK. The approach included documentary analysis, student focus groups and, interestingly, a «student study day», during which the outcomes of the research were intensively discussed with the student target group. The article summarizes its outcomes in three «Practice Points»:

«Students and academic staff have different perceptions of what constitutes research and the research skills that will be acquired from specific projects.

To fully benefit from research opportunities and develop essential skills, undergraduate students must be given training in «what research is» and project descriptors should be explicit about the research skill development opportunities provided.

Medical students should engage with research from the initial stages of their undergraduate education, and medical educators must facilitate significant student engagement with research and associated skills.»

## Conclusion

In this article an overview has been given of the important position of «research competencies» as part of a much wider array of medical competencies that a medical doctor must be able to employ in an integrative way in his or her professional practice. Therefore, research competencies are part of medical curricula all over the world. The educational approaches and methods that can be employed to enable students to achieve these competencies vary very much. Healey»s framework of research education offers a strong tool to analyse these different methods and make appropriate curriculum choices. Finally, the importance of evaluation of research education is stressed. Student perceptions play a key role in these evaluation efforts.

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# XXVII INTERNATIONAL SYMPOSIUM ON MORPHOLOGICAL SCIENCES «CELL, TISSUE, ORGANS – EXPERIENCE, INNOVATION AND PROGRESS»

(Post-release based on the materials of the XXVII International Symposium of Morphological Sciences, held in Kazakhstan)

Modern science is developing at a rapid pace and today, especially during the epidemic situation, scientific events are in demand, which allow us to consider topical issues that interest participants from different areas, individual ways to solve the same problem, listen to lectures by invited experts, and establish valuable contacts. **On May 27-31, 2021 in Almaty, Kazakhstan**, on the premises of the al-Farabi Kazakh National University, Higher School of Medicine, the Department of Fundamental Medicine, and the Eurasian Association of Morphologists held the XXVII International Symposium of Morphological Sciences ISMS 2021. This Morphological Congress was held, the first time, in 1971, in Mexico City, with the subsequent editions organized every two years in Argentina, Israel, the USA, Brazil, Portugal, Italy, Japan and many other countries (https://www.symposiamorphologica.com/).

The decision to hold the Symposium in 2020 in Kazakhstan was made at the meeting of the International Committee of Symposia on Morphological Sciences (ICSMS) on June 5, 2018 in Prague (Czech Republic) as a part of the XXVI International Symposium of Morphological Sciences. The advantage of votes over other candidate countries (South Africa, Argentina) allowed Kazakhstan to take a huge responsibility for holding this Forum.

Key words: cell, tissue, organs.

The main purpose and objectives of the Congress: to broadcast the latest achievements of morphological science in the world, to discuss global problems and prospects for the development of morphological research and to develop ways to unite and find collaborative opportunities between the CIS countries, Europe and Central Asia.

ISMS 2021 was a platform for broadcasting lectures, reports, and round tables dedicated to current issues and the latest achievements of medical science based on accurate morphological evidence of research. ISMS 2021 was held for the first time on the territory of the Commonwealth of Independent States (CIS), marking a new way of collaboration of scientists in the conditions of the emerging (epidemic) situation in the search for new methods and generation of ideas.

ISMS 2021, for the first time in Kazakhstan, brought together scientists from all continents, more than 500 participants, scientists from 40 countries of the world, opening up new prospects for cooperation. Moreover, the platform has united several countries in scientific teams that contribute to the fruitful exchange of scientific ideas and strengthen ties that will serve as a basis for Kazakhstan's scientific research to enter the scientific world.

The Congress, in view of the current pandemic situation, was held in an online format, so only Kazakh (local) academic authorities and anatomists and the representative of the Italian Embassy in Kazakhstan, Martino Castellani, Director of the Almaty Office of the Italian Trade Agency ICE, were present face-to-face at the congress venue. At the opening of the Congress, Mr. Castellani conveyed the congratulations from the Italian Ambassador in Kazakhstan, Mr. Pasquale D'Avino: «...I am extremely happy to send my congratulatory message to the participants of the XXVII International Symposium of Morphological Sciences, which will be held at the al-Farabi Kazakh National University, one of the most prominent and well-known institutions of higher education in the country and throughout Central Asia... I would like to express my gratitude for the opportunity to share this welcome address with the entire


Scientific Committee and the community of participants of the International Symposium, and in particular with the Coordinator for Scientific Relations, Professor Guido Macchiarelli from the University of L'Aquila, as well as with all Italian academicians and scientists for their contribution to maintaining a lively and dynamic cooperation between Italy and Kazakhstan...» (transcribed with permission).



The work of the Symposium began with a welcome speech by the rector of the al-Farabi Kazakh National University, Professor Zhanseit Tuymebayev. The coordinator and main host of the Symposium was the President of ISMS 2021, Assoc. Professor Gulmira Zhurabekova.



The Forum was attended by scientists from far abroad: President of ICSMS, Professor Guido Macchiarelli, Professor of Anatomy, Director of the Department of Life, Health and Environmental Sciences of the University of L'Aquila (L'Aquila, Italy); [15]



IFAA President, Emeritus Professor Beverley Kramer, Faculty of Health Sciences, University of the Witwatersrand, South Africa; [11] Professor Sherif Karam, Department of Anatomy, College of Medicine and Health Sciences, University of the United Arab Emirates (United Arab Emirates); [12] [13] Serena Bianchi, MD, PhD, Associate Professor of Human Anatomy, Department of Life, Health and Environmental Sciences, University of L'Aquila, Italy; [4] [5] Professor Mahmoud Farid Mahrous Bathalla, Al-Azhar Medical University Hospitals, Department of Neurosurgery, (Cairo, Egypt); Professor Zhanna Mussazhanova, (Nagasaki, Japan); Hendrik Mathijs Jozef Frencken, Senior Education Consultant, ICLON, Graduate School of Teaching, Leiden University (Leiden, the Netherlands); Masahiro Nakashima, MD, PhD, Professor and Head of the Department of Diagnostic and Tumor Pathology, Head of Tissue and Histopathology section, Department of Data Registry, Atomic Bomb Diseases Institute, Nagasaki University, (Nagasaki, Japan); Stefania A. Nottola, MD, PhD, Professor, Department of Anatomy, Histology, Forensic Medicine and Orthopedics, Section of Human Anatomy, Electron Microscopy Unit, Faculty of Pharmacy and Medicine, University of La Sapienza, Italy; [1] [2] [15] Professor Diogo Pais, MD, MSc, PhD, Professor and Chairman of the Department of Anatomy, NOVA Medical School, NOVA University of Lisbon, Portugal; Dr. Nuno Domingues, MD, Urologist, Member of the European Council of Urology, Human Cadaveric Course Coordinator, NOVA Medical School, NOVA University of Lisbon, Portugal; Dr. Mohamed Mahmoud Farghali, Consultant of Obstetrics and Gynecology, Maternity Hospital, Sabah area, Shuwaikh, Kuwait; Maria Grazia Palmerini, PhD, Associate Professor, Department of Life, Health and Environmental Sciences, University of L'Aquila (L'Aquila, Italy); Professor Jose Sanudo, Department of Human Anatomy, Complutense University, (Madrid, Spain); Dr. Erin Hutchinson. Faculty of Health Sciences, University of the Witwatersrand, South Africa; Dr. Carol Hartmann, Faculty of Health Sciences, University of the Witwatersrand, South Africa. [9] [10]

Lectures, round tables, mini-symposia, master classes on current topics and, naturally, breakout sessions were organized http://www.isms2020.kz/ index.php/final-program.

The lectures of the invited speakers were welcomed and applauded.

For anatomists, histologists, biologists, pathomorphologists, physiologists (May 28 at 12.00, Nur-Sultan time), a lecture was offered by a leading scientist, Professor Sherif Karam of the University of the UAE (United Arab Emirates) on the topic:»-Gastric stem cell biology in health disease».



Professor Sherif Karam, Department of Anatomy, College of Medicine and Health Sciences, UAE University (United Arab Emirates). Professor Sherif Karam deserves to be thanked for constantly updating the data on the study of the stomach and transmitting this knowledge.

Especially for pathomorphologists (May 29 at 12.00, Nur-Sultan time) Professor Masahiro Nakashima, PhD, a leading scientist from Japan, offered a lecture on the topic: «Molecular pathology of nodule in nodule type thyroid follicular tumors».



Professor Masahiro Nakashima, Head of Department of Tumor and Diagnostic Pathology, Head of Tissue and Histopathology Section, Division of Data Registry, Atomic Bomb Disease Institute, Nagasaki University, Nagasaki, Japan. Professor Masahiro Nakashima gave interesting fresh data on the study of thyroid cancer, which was of utmost interest for the large number of specialists in this field, which attended his lecture. [3] [14]

Professor Hendrik Mathijs Jozef Frencken, Senior educational consultant. ICLON, graduate school of teaching (retired), Leiden University (Leiden, Netherlands) delivered a very interesting lecture on the topic' «Professional development for teachers in the medical faculty: the use of educational models». The problems of teaching, the organization of our usual duties in the educational process has significantly undergone difficulties in connection with the transition to the online system. Professor Hendrik Frencken's lecture on the educational process in medicine provoked an active response from the audience.



Scientific reports were presented at 6 sections, traditionally held within the framework of the congress, including new directions.

The topic: «Organ and system; tissue and cell morphology; cardiovascular science; neuroscience» with the preliminary lecture: «Gastric stem cell biology in health disease» should be noted (section 1, 4 reports). A unique tandem of two scientists from different countries, moderator of the section Professor Serena Bianchi and guest lecturer Professor Sherif Karam, were able to attract about 200 students to the section, which was applauded with large participation of the audience.

A large number of speakers (12) and listeners (40) were united in the topic: «Clinical anatomy; morphological aspects of the somatic pathology; cell biology and biochemistry in the modern clinical research» (section 2).

The topic «Biology of reproduction» was developed in section 3 (6 speakers, 40 listeners). Reproductive morphology is one of the most interesting and inexhaustible scientific areas, so this section was very informative. Professor Ibrahim Abdelazim started by giving a very interesting lecture on the surgical anatomy of the female genital tract, and Professor Dr Mohamed Mahmoud Farghali moderated the section very efficiently, despite being busy at the clinic.

Poster presentations (section 4-9 speakers, 25 listeners and section 5-13 speakers, 40 listen-

ers) were received with great interest. The team of moderators of the poster sections, scientists of various fields Professors Gaziza Smagulova, Mahmoud Farid and Sergey Liashchenko, were able, with their expertise, to make the poster sections very useful and informative.

The section **«Medical Education»** was created at the request of scientists in view of the relevance of the topic and the need for exchange. Due to the high interest of representatives of different universities in participating, this section on **«Problems and solutions of online teaching in the pandemic situation in the Medical schools in the World»** was converted into the category of «round table». Five speakers, representatives of six medical universities and 50 students participated in the discussion. We thank the moderator, Professor Gulmira Derbissalina, for a very stimulating discussion.

For the first time, the ISMS Congress also included meetings of young scientists (section 6, Young scientists contest and the Student poster section). Thanks to the active participation and moderation of Professor Maria Grazia Palmerini in the student sections, the communication turned out to be very fruitful. As part of the student events, a master class was held on the topic «Immunofluorescence analvsis of DNA damage response protein p53-binding protein 1: molecular indicator of genomic instability in human carcinogenesis» by Professor Zhanna Mussazhanova. The topic of the master class was of great interest for young scientists. The international jury of the International Student Contest determined the two best student reports: Abdul Razaq Imran Khan (Dubai, United Arab Emirates) and Valeriy Ignatyev (Aktobe, Kazakhstan)

Another debut in International Symposia of Morphological Sciences was a round table on the topic **«Body donation: a global perspective in a round table discussion»** with information from 10 distinguished anatomists from different countries about the problems of providing human cadavers to the educational process, bringing together 35 participants. We thank Professor Beverley Kramer and the participants of the round table Umit S. Sehirli, Sagimova Gulzira, Brendon Billing, Francesco Cappello, Susana N. Biasutto, Sapargali Rakhmanov, Hong-Jin Sui, [6] [7] [8] Stefania A.Nottola, Diogo Pais, Tamara Abayeva.



Within the framework of the symposium, a unique **Workshop** was also held by Portuguese scientists from the NOVA University (Lisbon) on «Laparoscopic **minimally invasive surgery -hands-on courses on human cadavers**». The Portuguese scientists demonstrated the high importance of practicing surgical skills on cadavers to reduce technical errors and prevent complications of work in the clinical practice as a surgeon. Special thanks to Professor Diogo Pais and his colleague Dr. Nuno Domingues for the opportunity to listen, obvserve and learn a lot!

All scientific abstracts are published in the journal **«Annals of Anatomy»**, indexed in the databases Science Citation Index, Scopus, PubMed/ Medline, providing students with a unique opportunity to publish their research in a rating publication http://www.isms2020.kz/index.php/call-forabstracts.

We express our gratitude to the scientists, members of two major international organizations ICSMS and IFAA headed by the scientists Professor Guido Macchiarelli and Emeritus Professor Beverley Kramer for their help in organizing all scientific events within the framework of the Congress.



Sincere words of gratitude to the Honorary President of ISMS 2021, Professor Yerbol Bekhmuhambetov, Chairman of the Board of the United Association of Individual Entrepreneurs and Legal Entities «National Chamber of Health» (Nur-Sultan, Kazakhstan) for supporting the idea of holding the congress in Kazakhstan, Honorary President, Professor Raushan Issayeva for assistance and advice in organizing the congress, and the main coordinator and host of the Symposium, President of ISMS 2021, Professor Gulmira Zhurabekova.

### Conclusion

The XXVII International Symposium on Morphological Sciences, held in Almaty, Kazakhstan, from 27-31 May, 2021, provided five eventful days of presentations by experts from different fields in morphology, the opportunities to exchange experiences, to develop new friendships and professional network, with a very special atmosphere of the world of science, demonstrating that communication between scientists in the modern world is a real necessity, contributing to the development of solid morphological scientific foundations in Kazakhstan as in the world of Anatomy.

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