Mental health support to perinatal women with COVID-19 pneumonia, intensive care unit and post-intensive care syndromes

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Abstract

Intensive care unit syndrome and post-intensive care unit syndrome became one of urgent and global problems of current medicine. Their development is associated, among other causes, with the specific environment and modalities of an ICU in combination with COVID-19 pneumonia which could have adverse effect on the mental health of patients. This cross-sectional, hospital-based study was conducted in December 2020 - January 2022 in the cohort of 677 perinatal women with mental health disorders associated with severe and critical COVID-pneumonia. They were recruited at the Maternity Hospital ICU of the National Specialized Versatile Medical Center Zangiota-1 in Tashkent, Uzbekistan. Most patients had post-traumatic stress disorder (56.6%; 383 of 677). Generalized anxiety disorder was diagnosed in 26.7% (181 of 677) while depressive conditions were found in 16.7% (113 of 677) of cases. In the postpartum period, PTSD, anxiety, and depression combinations were identified in 46.1% (312 of 677) of cases according to the PHQ-ADS combined scale; it was typical for women with severe and critical COVID-19 in trimester 3 of pregnancy. The therapy for mental health disorders in perinatal women was focused on reducing the frequency of threats of pregnancy loss, ICUS, and PICS development. Psychotherapy was supplemented with sedative and metabolic drugs. After discharge from the hospital ICU (n=613), an individual rehabilitation program was made for each of them. By month 8 all women have been successfully rehabilitated and had no signs of mental health disorders. An effective therapeutic tactics for mental health disorders and differentiated psychotherapy as well as delivery in a specialized medical center may improve significantly the pregnancy outcomes and shorten the rehabilitation period.

Keywords: *COVID-19 pandemic; intensive care; perinatal women; post-traumatic stress; anxiety; depression*

Abbreviations: DEAS - depression-excitation assessment scale, GAD – generalized anxiety *disorder,* ICUS - intensive care unit syndrome, IES - Impact of Event Scale-6, MHD – mental health disorders, MOF - multiple organ failure, NVP – nausea and vomiting during pregnancy, PICS – post-intensive care unit syndrome, *PRA* - pregnancy-related anxiety, PRD - pregnancy-related depression; PTSD – post-traumatic stress disorder, SAPS - Simplified Acute Physiology Score, STAI - Spielberger State-Trait Anxiety Inventory,

Introduction

An inevitable, though expected, consequence of advances in intensive care technologies is the effect of specific environment and modalities of an intensive care unit (ICU) on the mental health of patients that increases the disease burden. That is why Intensive Care Unit Syndrome (ICUS) and Post-Intensive Care Syndrome (PICS) became one of urgent and global problems of current medicine.

This study is a part of a larger one conducted at the same health care setting and at the same time on 3080 pregnant women hospitalized with mild to critical COVID. The present study recruited 677 perinatal women treated in the maternity hospital ICU. They all had transient mental health disorders (MHD); therefore, our research was focused on ICUS and PICS syndromes manifested by Post-Traumatic Stress Disorder (PTSD), pregnancy-related anxiety (PRA), and pregnancy-related depression (PRD).

Back in 1985 the ICUS was defined as one of organic

brain syndromes manifested by "fear, anxiety, depression, hallucinations, and delirium." [1] A. Luetz et al. (2019) demonstrated that this condition affected up to 80% of ICU patients and could be a predictor of long-term cognitive impairment [2].

PICS is used to term "the new or worsening impairments in physical, cognitive, or mental health status arising after critical illness and persisting beyond acute care hospitalization" [3]. Both ICUS and PICS cover psychological, cognitive and physical disorders (e.g., polyneuropathy, respiratory dysfunction, muscle and joint atrophy, etc.). ICUS also manifests itself as difficult for patient's ventilator weaning, speaking or swallowing. Currently, these two syndromes are highlighted due to a long stay of patients with severe and critical COVID-19 pneumonia in an ICU and their subsequent long rehabilitation in the post-COVID period [4-7].

The problems of ICUS and PICS management are particularly urgent in pregnant and postpartum women with COVID-19 pneumonia who have several psychosomatic and cognitive factors aggravating each other. The number of COVID-patients, who survived owing to intensive therapy, is increasing and ICUS and/or PICS treatment is elaborated. However, there is a lack of data on long-term monitoring and studying the psychopathological indicators for pregnant women with COVID-19 pneumonia treated in an ICU which may provide appropriate ground for the future planning of socio-psychological strategies of perinatal women support.

Methods

This cross-sectional hospital-based study has been conducted from December 2020 to January 2022 in the cohort of 677 women in antenatal and postpartum periods with COVID-19 pneumonia who were recruited at the maternity hospital ICU of the National Specialized Versatile Medical Center Zangiota-1 in Tashkent, Uzbekistan.

The objectives of the research were studying the psychosomatic disorders, assessment and treatment of the psychological disorders of pregnant and postpartum women with COVID-19 pneumonia treated in the ICU. Eligible participants were: (1) pregnant women aged 18-40 years; (2) postpartum women (one week after childbirth) from the same age-group; (3) patients who provided written informed consent before their enrolment. If an initially involved woman turned to have previously existing psychiatric disorders, she was excluded.

The participating women were asked to complete anonymously standardized questionnaires and scales to assess their mental health disorders (MHD), namely Post-Traumatic Stress Disorder (PTSD), pregnancy-related anxiety (PRA), and pregnancy-related depression (PRD).

The Spielberger State-Trait Anxiety Inventory (STAI) was used to assess the level of situational and personal anxiety of pregnant women with nausea and vomiting during pregnancy (NVP). Another instrument was the updated version of the Prediction-Unique Quantification of Emesis scoring system (PUQE-24) where the severity of NVP is assessed by three clinical symptoms: nausea, vomiting and urge to vomit during the previous 24 hours. The scale of assessment of depression - excitation (DEAS) and Psychological Evaluation Test (PET) were also used.

To compare the obtained information the criteria of "sensitivity" and "specificity" proposed by Fletcher et al. were used [8]. The sensitivity and specificity of questionnaires IES-6, GTR-7 and PHQ-9 scales were checked out before identification and assessment of the dynamics of PTSD, anxiety and depression.

The PTSD scale assessment showed that sensitivity of the IES-6 related to points 2 and more was 83.14%, and the specificity of the method was 98.04% (95%, CI=96.6-99.0; p<0.001). The optimal criterion for the diagnosis of PRA in COVID-19 is 5 or more points by GAD-7 scale [9]. According to our data, the sensitivity associated with this criterion is 77.79% with 95.92% specificity (95%, CI=76.1-79.4, p<0.001). The optimal criterion for detecting PRD in COVID-19 was 10 points or more. According to our data, the sensitivity associated with this criterion is 94.33% with 89.4% specificity (95%, CI = 86.7-91.7, p < 0.001).The predictive value of a positive result determined the proportion of examined women who had a real positive result on the test under study among the total number of subjects who had a positive result.

Statistical analysis of the findings was performed using Statistica 6.1, USA. The value of statistical significance (p) is taken equal to 0.05. ontinuous values were presented as mean ±SD under the normal distribution law. Categorical data are presented as fractions, frequencies and percentages.

Results

The patient condition was defined according to the Clinical Spectrum of SARS-CoV-2 Infection-2022 [10]. The overwhelming majority of patients (72.4%; 490 of 677) had severe COVID-19 (SpO$_2$ <94% on room air at sea level, PaO$_2$/FiO$_2$ <300 mm Hg, a respiratory rate >30 breaths/min, or lung infiltrates >50%. Bilateral pneumonia was diagnosed in 48.0% of recruited women; in most of them (60.0%), MSCT

showed lung infiltrates up to 50%. Forty-one per cent of patients were critically ill, *i.e.* they had respiratory failure, septic shock, and/or multiple organ failure (MOF) [ibid].

Mental health assessment

According to special questionnaire scales the mental health disorders in the ICU patients were as follows: PTSD was found in 56.6%; (383 of 677), while 26.7% (181 of 677) suffered from generalized anxiety disorders (GAD), and PRD was diagnosed in 16.7% (113 of 677) of cases. The PHQ-ADS combined scale identified combinations of PTSD, PRA and PRD in 46.1% (312 of 677) of cases which was typical for women with severe and critical COVID-19 resulted in premature birth, miscarriage and perinatal mortality. PTSD and combined disorders are the most difficult-to-treat types of MHD in pregnant women with COVID-19 pneumonia. This condition is also characterized by multiple organ failure (MOF); its incidence was 41.0% (277 of 677). Most of them (75.4%; 209 of 277) were women in the third trimester of pregnancy with severe COVID- pneumonia (61.4%; 170 of 277).

Taking into account the adverse effects of MHDs on ICU perinatal patients and importance of their early management the following risk factors of ICUS development were identified:

- the ICU environment (sleep disturbance due to excessive light and noise, fears related to the severity of their condition); it had a bad impact on 234 (84.5%) patients;
- autonomic disorders and polyneuropathy such as nausea and vomiting of pregnancy, delirium; they were reported in 155 (55.9%) patients;
- metabolic and hypoxic disorders, e.g., diabetes mellitus, metabolic syndrome, which were found

in 103 (37.2%) patients;

- too many diagnostic and therapeutic procedures; they expectedly affected the emotions of almost all conscious patients;
- adverse effect of some drugs, sometimes individual, e.g. sedatives, antidepressants, etc., was observed in 5 (1.8%) patients.

Early signs of ICUS were speech agitation (165/59.5%), unexplained depression (176/63.5%), inadequate requests or acts (56/20.2%).

The following actions contribute to ICUS prevention or at least mitigate its manifestations:

• contacts with patients before admission to an ICU, if possible;

• analgesia given in advance;

• sedation and tranquilization;

• combination of treatment actions to reduce their number;

• special attention to patients on mechanical ventilation;

• participation of a psychotherapist if necessary;

The mortality rate in the ICU was 9.4% (64 out of 677). The majority of deaths (68.8%; 44 cases) were women with critical COVID-19 and combined MHD.

In severe MHD in perinatal women with COVID-19, the effectiveness of etiotropic and pathogenetic treatment (correction of coagulopathy, respiratory and antibacterial therapy) directly depends on the proper psychosocial support of patients.

In half of pregnant women and women in labor with PTSD (204 of them 312; 53.3%), progression of pathology was noted, in women with anxiety syndrome, progression was noted in only 21.5% (39 of 181) of cases, and improvement in 78.5% (142 out of 181) patients (p=0.03) (table 1).

Table 1: MHD improvement/aggravation in perinatal women with COVID-19 pneumonia during treatment at ICU

Mental health	Improvement	Aggravation	Total (n = 677)
PTSD	179 (46.7%)	204 (53.3%)	383 (56.6%)
PRA	142 (78.5%)	39 (21.5%)	181 (26.7%)
PRD	79 (70.0%)	34 (30.0%)	113 (16.7%)
Combined disorders	127 (40.7%)	185 (59.3%)	312 (46.1%)

After recovery of ICU patients and their discharge from the hospital (n=613), an individual rehabilitation program was made for each of them taking into account the risk factors. Monthly examination of patients (at hospital or by telephone call) with the IES-6 scale (to assess the PTSD) and the combined PHQ-ADS scale (to assess PRA/PRD) gave information on the rehabilitation level in the groups of patients who had moderate (n=111), severe (n=472) and critical (n=30) COVID-19 pneumonia. The rehabilitation level was also determined in the group of patients experienced MOF (n=277). The patients were considered to have good rehabilitation with a score less than 19 on the IES-6 scale (elimination of PTSD)

and a score less than 2 on the combined PHQ-ADS scale (no PRA and PRD).

The effectiveness of MHD rehabilitation in the moderate COVID-19 group of women treated at ICU was better than in the group with severe and critical COVID-19 pneumonia. For instance, the moderate cases completed rehabilitation at month 4 after their discharge from the hospital, while patients with severe pneumonia needed another 4 months after discharge to complete rehabilitation. After MOF, 213 recovered women completed successfully the rehabilitation course much later than all others. Thus, MOF aggravated the MHD clinical picture and prolonged the rehabilitation period due to the development of ICUS and PICS.

Discussion

It is generally accepted that COVID-19 morbidity in pregnant women is higher than in general population. COVID-19 infection mortality among pregnant women reaches 25%; the frequency of premature birth ranges from 4.3 to 5.0%, preeclampsia occurred in 5.9%, miscarriages give 14.5%, premature rupture of the membranes and fetal growth delays were reported in 9.2% and 2.8-25.0%, respectively [11]. Moreover, the WHO reports that 6% to 10% of COVID-19 patients have a severe to critical infectious disease and may need to be admitted to the ICU [12].

The short-term outcomes of treating patients in well-equipped ICU have improved for over the past fifty years. However, many ICU survivors often face persistent physical and mental health disorders following their critical illness recovery. Pathogenesis of MHDs in COVID-19 is directly related to severe respiratory failure with development of hypoxic and hemic hypoxia. In addition, the MHD manifestations in COVID-patients are associated with the stressful situation due to the pandemic and the direct impact of the virus on the nervous system of patients. Prolonged immobilization under the necessity and inflammatory cytokines activates the ubiquitin-proteasome system, autophagy-lysosome system, and other intracellular pathways increasing the levels of proteolysis and catabolism. It usually manifests clinically as the sarcopenia and myopathy [13]. Neuropathy often developing in COVID-19 patients is thought to occur due to microvascular ischemia which causes demyelination through neuronal mitochondrial function [14]. The pathophysiologic mechanisms underlying the cognitive disorders associated with PICS probably are caused by microglial activation, oxidative stress, dysfunction of mitochondria, and activation of apoptotic pathways [15]. Neuro-inflammation is supposed to play some role because higher levels of IL-6 and IL-10 were found in people with a decreased cognitive ability even 4 years after their discharge from ICU [16].

The factors that cause MHD in ICU patients are known; they include: "(1) pre-admission history; (2) past ability to adapt to stress; (3) past and current medications; (4) current clinical status; and (5) environmental factors" [7].

Durankus F. et al. found that over 1/3 of the perinatal women had PRD during the pandemic [17]. Interestingly, the research conducted in China showed that the official declaration of pandemic increased the risk of depression in the group of women who "were primiparous, younger than 35 years, underweight before pregnancy, employed full time, in middle income category, and had a per capita living area of ≥20 m^2 and decreased physical activity", i.e., had rather good quality if life [18]. The GAD prevalence in pregnant women was reported to be 3–4 times greater than in the general population due to the COVID-19 pandemic [19]. Up to 72% of pregnant women had combined anxiety and depressive symptoms [20]. The prevalence of PTSD in perinatal women varied from 0% to 43% before the pandemic [21]. In our study, it was 56.6%.

Currently, researchers propose various modalities to improve management of COVID-positive pregnant and postpartum women with MHD. Among them, there are: universal screening of pregnant women for COVID-19 before admission to maternity facilities [22], the online Mindfulness-Based Stress Reduction (MBSR) program that can be used to reduce stress, anxiety and fear of delivery [23]. In addition, it turned out that pregnant women were significantly more likely to need treatment in an ICU [adjusted risk ratio (aRR): 1.5, 95% confidence interval (CI): 1.2-1.8] and receive mechanical ventilation (aRR: 1.7, 95% CI: 1.2-2.4) [24]. The CDC report supported these findings and, which is more, identified an increased risk for needing extracorporeal membrane oxygenation (ECMO) cannulation (0.7 vs. 0.3 per 1000 cases; aRR: 2.4; 95% CI: 1.5-4.0) [25].

ICUS and PICS including PRA, PRD, and PTSD may be mitigated by the implementation of some ICU practices [6]. Hence, the earlier MHD is recognized, the better is the prognosis. The traditional ICUS treatment tactics is aimed at: (1) elimination or at least correction of causative factors including the environmental stress; (2) proper choice, dose, and route of administration of sedative and antipsychotic agents; (3) frequent patient and family communication [7]. A more detailed approach is the ABCDEF Bundle which is used at over 70 US

hospitals [26].

It is an evidence-based set of interventions started by ICU staff immediately after patient's admission to prevent ICUS and PICS. ABCDEF is decoded as:

- A- Assessment, management, and prevention of pain

- B- Both spontaneous breathing trials and spontaneous awakening trials

- C- Choice of sedation and analgesia (maintain a relatively light level of sedation and avoid benzodiazepines)

- D- Delirium assessment, prevention, and management

- E- Early mobility and exercise

- F- Family engagement and empowerment

It us generally accepted that during the pandemic specific infection hospital environment, including an ICU, can give an impetus to or aggravate MHDs that are associated with COVID-19 or were previously latent. To reduce the risk factors and improves outcome Kramer CL (2017) suggests less aggressive sepsis treatment and early mobilization [27].

In addition to medication, Luetz A. et al. (2019) suggest to develop innovative approaches to transform standards of ICU room design to remove, or at least minimize, potential stressors [2]. The main solution of this problem does not require expensive architectural modifications: these are proper equipment, light control, floor planning, and, which is the most important, the staff trained in early recognition and coping with the first signs of ICUS and PICS.

Conclusion

Early identification and treatment of ICUS and PICS significantly mitigate somatic and obstetric complications that may develop in these patients. Significant predictors of MHD development are: more than 40 SAPS II points, severe and critical COVID-19, two or more miscarriages in the history, trimester 3 of pregnancy. Combined MHD and MOF aggravate the patient's condition and prolong the rehabilitation period.

The therapeutic tactics for MHD in perinatal women with COVID-19 pneumonia reduces the threats of pregnancy loss, gestosis, weakness of labor activity, early amniotic fluid discharge, etc. Differentiated psychotherapy supplements sedative and metabolic drugs, permanent tocolytic therapy, and physiotherapy courses as well as delivery in a specialized medical center.

Early identification of ICUS and PICS by the ICU staff improves the prognosis for perinatal women with MHD.

Ethics approval and consent to participate

The Ethics Committee of Zangiota-1 hospital (Tashkent, Uzbekistan) approved this study. We confirm that all methods we used were performed according to the relevant standards and regulations. We confirm that all the explanations related to the participation in the study and written informed consent form were provided to the recruited women before they filled in the anonymous questionnaires.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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