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UNVEILING THE HETEROGENEOUS BURDEN OF LONG COVID IN THREE IRANIAN CITIES

MOUSAVI M.J¹, AMIRZARGAR S.², AREFINIA N.³, AJEL M.⁴, ARYAMAND S.⁴, BEHBOUDI E.^{4*}

¹ Department of Hematology, School of Para-Medicine, Bushehr University of Medical Sciences, Bushehr, Iran

² Islamic Azad University Roodehen branch, Azad, Iran

³ Bio Environmental Health Hazards Research Center, Jiroft University of Medical Sciences, Jiroft, Iran

⁴ Department of Basic Medical Sciences, Khoy University of Medical Sciences, Khoy, Iran

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ABSTRACT

The COVID-19 pandemic has left an enduring global health legacy, extending far beyond the acute phase of the illness. A significant proportion of individuals, even after recovering from the initial infection, experience a constellation of persistent symptoms, a condition known as Long COVID or Post-Acute Sequelae of SARS-CoV-2. This study investigates the heterogeneous burden of Long COVID in three distinct cities in Iran: Khoy, Bushehr, and Jiroft, each presenting unique geographical, socioeconomic, and healthcare contexts. Employing a cross-sectional study design, we surveyed 900 individuals in three cities of Iran, providing valuable insights into the prevalence, risk factors, and symptomatic manifestations of Long COVID. In the present study, Jiroft presents the highest prevalence of Long COVID at 24%, closely followed by Khoy at 21.7%, while Bushehr shows a considerably lower rate of 16%. The age, gender, pre-existing condition, and vaccination were significantly different among these three cities (p -value less than 0.05). Individuals in Jiroft exhibited a greater burden of pre-existing conditions, experienced more severe initial infections, were less likely to have access to health insurance, and reported a high financial burden of health care. This study suggests a convergence of vulnerabilities contributing to the city's higher Long COVID prevalence. Symptom profiles also varied across the cities, but the core complaints remained prominent, including fatigue, shortness of breath, and cognitive dysfunction. By identifying the specific drivers and patterns in each city, we can inform tailored interventions, healthcare resource allocation, and public health strategies that are responsive to the unique contexts of Khoy, Bushehr, and Jiroft.

KEYWORDS: long covid, Iran, risk factors, symptoms.

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ADDRESS FOR CORRESPONDENCE:

Emad Behboudi, PhD, Assistant Professor
Khoy University of Medical Sciences
Valiasr street, Khoy 8144168859, Iran
Tel.: +98 (936) 7011199
Email: emadbehboudi69@gmail.com

INTRODUCTION

The COVID-19 pandemic has left an indelible mark on global health, with millions of individuals experiencing lingering symptoms long after the acute phase of the infection has resolved [Zandi et al., 2021]. This phenomenon, commonly referred to as Long COVID, has emerged as a significant public health challenge, characterized by a wide array of physical, cognitive, and psychological symptoms that persist for weeks or months [Davis et al., 2023, Gold et al., 2021]. “Long COVID” is a commonly used term to describe what the World Health Organization (WHO) defines more formally as post COVID-19 condition. Post COVID-19 condition is, according to WHO, in patients with a history of possible or confirmed SARS-CoV-2 infection, usually three months from the onset of COVID-19, with symptoms for two months and not explained by a different diagnosis [Malambo et al., 2024]. While the global focus has largely been on understanding and mitigating the acute effects of the virus, the long-term consequences of COVID-19 remain understudied, particularly in low- and middle-income countries [Huang et al., 2023, Golzardi et al., 2024, Teimouri et al., 2022].

Long COVID presents with a wide range of symptoms, which can vary significantly among individuals. Common clinical symptoms include persistent fatigue, shortness of breath, chest pain, and cognitive impairments such as memory loss and difficulty concentrating, often referred to as “brain fog.” Additionally, many individuals report musculoskeletal pain, headaches, cardiovascular issues such as palpitations, and in some cases, ocular manifestations [Sudre et al., 2021, Teimouri and Rasoulinejad et al., 2022]. Psychological symptoms, including anxiety, depression, and post-traumatic stress disorder, are also prevalent, further complicating the clinical picture. These symptoms can persist for months, severely impacting the quality of life and productivity of affected individuals [Mousavi et al., 2025, Negrut et al., 2024].

Risk factors for developing Long COVID are multifaceted and include both demographic and clinical variables. Older age, female gender, and the presence of pre-existing conditions such as obesity, diabetes, and cardiovascular diseases have been identified as significant risk factors [Behboudi et al., 2021, Greenhalgh et al., 2020, Nikoo et al.,

2024]. The severity of the initial COVID-19 infection also plays a crucial role; individuals who experienced severe acute symptoms or required hospitalization are more likely to develop Long COVID [Chen et al., 2022]. Socioeconomic factors, such as access to healthcare and occupational exposure, further contribute to the risk, highlighting the need for a comprehensive approach to understanding and mitigating this condition [Xie et al., 2022].

Despite the growing global literature on Long COVID, limited studies have investigated its prevalence and associated risk factors in Iran, particularly across cities with varied socioeconomic, geographic, and healthcare characteristics [Asadi-Pooya et al., 2021, Tazeh et al., 2022, Farshidgozar et al., 2024]. This study aims to examine the prevalence, symptom profiles, and risk determinants of Long COVID in three socioeconomically distinct Iranian cities: Khoy, Bushehr, and Jiroft. These cities represent diverse environmental conditions, levels of healthcare access, and economic contexts. By capturing these localized patterns, the study addresses a critical knowledge gap regarding the long-term consequences of COVID-19 in low- and middle-income settings. The findings are intended to inform tailored public health strategies, equitable healthcare planning, and future research focused on context-specific interventions both within Iran and in comparable regions globally.

MATERIALS AND METHODS

Study Design and Setting: This cross-sectional study was conducted in three Iranian cities—Bushehr, Khoy, and Jiroft—selected for their diverse demographic, socioeconomic, and environmental characteristics. These cities represent a broad spectrum of urban populations in Iran, providing a comprehensive overview of the heterogeneous burden of Long COVID. Data were collected over 3 years, from 2021 to 2024, to capture a wide range of post-COVID-19 experiences among individuals who had tested positive for SARS-CoV-2 at least three months prior to the study. The study protocol was approved by the Ethics Committee of Khoy University of Medical Sciences, and written informed consent was obtained from all participants. Confidentiality of data was maintained throughout the study, and participants were assured that their information would be used solely for research purposes.

Study Population and Sampling: The study population included adults aged 18 years and older who had recovered from acute COVID-19 infection, confirmed by a positive polymerase chain reaction test. Participants were recruited through a combination of hospital records, community health centers, and online platforms to ensure a diverse sample. A stratified random sampling approach was used to ensure representation across age groups, genders, and socioeconomic statuses. Individuals with a history of severe psychiatric or neurological disorders prior to COVID-19 infection were excluded to minimize confounding factors.

Data Collection: Data were collected using a structured questionnaire administered through face-to-face interviews and telephone calls. The questionnaire consisted of three main sections:

1. **Demographic Information:** Age, gender, education level, occupation, and socioeconomic status.

2. **Clinical History:** Covering pre-existing medical conditions, severity of the acute COVID-19 infection (categorized as mild, moderate, or severe), hospitalization status, and treatments received.

3. **Long COVID Symptoms:** Participants were asked to report any persistent symptoms experienced after COVID-19 recovery. Long COVID was defined based on the clinical case definition proposed by the World Health Organization, which describes post COVID-19 condition as symptoms that begin usually within three months of the onset of confirmed or probable SARS-CoV-2 infection, persist for at least two months, and cannot be explained by an alternative diagnosis [Organization et al., 2021]. Only symptoms lasting 12 weeks or longer were considered in this study. Reported symptoms were categorized into three domains: physical (e.g., fatigue, shortness of breath, chest pain), cognitive (e.g., brain fog, memory loss), and psychological (e.g., anxiety, depression).

The questionnaire was developed based on a comprehensive literature review and refined through expert consultation. While formal psychometric testing (e.g., content validity ratio, content validity index, and test-retest reliability) was not conducted, content validity was ensured through review by five faculty members specializing in epidemiology, virology, and infectious diseases. A pilot study with 30 participants confirmed the clarity and relevance of the items.

Ethics Approval and Participant Consent:

The research protocol was reviewed and approved by the Khoy University of Medical Sciences Ethics Committee (Approval Code: IR.KHOY.REC.1402.049). All human participant procedures were conducted in accordance with the research committee ethical requirements at the institutional and country levels, and also consistent with the 1964 Helsinki Declaration and its later amendments or equivalent ethical standards. Every participant was informed of the purpose of the study, that participation is voluntary, and the right to withdraw at any point in time without penalty. Written informed consent was obtained from all the participants before data collection. Anonymity and confidentiality were maintained tightly, and all the data were used for research purposes only.

Statistical Analysis: Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 26. Descriptive statistics were used to summarize demographic and clinical characteristics. Prevalence rates of Long COVID symptoms were calculated and stratified by age, gender, and severity of acute infection. Multivariate logistic regression analysis was performed to identify risk factors associated with Long COVID, adjusting for potential confounders such as pre-existing conditions and socioeconomic status. A p-value of <0.05 was considered statistically significant.

RESULT

The table 1 shows the number of participants who developed Long COVID in each city based on the study of 300 individuals in each location. It presents both the raw count and the calculated percentage of the prevalence. In Khoy, 65 out of 300 participants developed Long COVID, a prevalence of 21.7%. In Bushehr, 48 out of 300 participants developed Long COVID, a prevalence of 16%, and in Jiroft, 72 out of 300 participants developed Long COVID, a prevalence of 24%.

TABLE 1.

Variable	Observed Prevalence of Long COVID.		
	City		
	Khoy	Bushehr	Jiroft
Total Participants	300	300	300
Number with Long COVID	65	48	72
Prevalence Rate of Long COVID (%)	21.7%	16%	24%

Table 2 outlines the count of individuals with specific risk factors among those who developed Long COVID in the study in each city. Severe Initial Infection: Jiroft has the highest count (18), followed by Khoy (12), and then Bushehr (10). Age 60+ Years: Jiroft shows the highest number (15), compared to 8 in Khoy and only 4 in Bushehr. Pre-existing Conditions: Jiroft has the highest count (29), followed by Khoy (24), and Bushehr with the lowest count (13). Diabetes and Hypertension were significantly higher than other pre-existing conditions. Female Gender: Khoy (40), Bushehr (30), and Jiroft (45) all have more women with Long COVID than men. Unvaccinated Status: Jiroft has the highest (28), then Khoy (18), and Bushehr (15). Interestingly, among these factors, age, gender, pre-existing condition, and vaccination were significantly different among these three cities ($p < 0.05$).

Table 3 illustrates the number of individuals who reported specific Long COVID symptoms in the study sample in each city. Fatigue was the most frequently reported symptom in all cities, with the highest count in Jiroft (60), followed by Khoy (50), and Bushehr (35). Shortness of Breath was

TABLE 2.

Distribution of Long COVID Risk Factors among 300 Participants in Each City.

Risk Factor	Khoy (n=65)	Bushehr (n=48)	Jiroft (n=72)	p-value
Severe Initial Infection	12	10	18	0.15
Age 60+ Years	8	4	15	0.04
Pre-existing Conditions	24	13	29	0.03
Respiratory Diseases	2	1	3	0.65
Diabetes	6	2	7	0.42
Kidney Diseases	1	0	2	0.32
Liver Diseases	1	1	2	0.75
Neurological Diseases	2	1	0	0.55
Psychiatric Disorders	0	2	1	0.60
Autoimmune Diseases	1	1	0	0.85
Infectious Diseases	1	0	1	0.5
Gastrointestinal Diseases	2	1	3	0.7
Skin Diseases	1	1	2	0.9
Hypertension	4	1	5	0.4
Bone Diseases	1	0	2	0.45
Eye Diseases	1	1	2	0.8
History of Cancer	1	1	0	0.7
Female Gender	40	30	45	0.01
Unvaccinated Status	18	15	28	0.04

TABLE 3.

Most Common Long COVID Symptoms among 300 Participants in Each City.

Symptom	Khoy (n=65)	Bushehr (n=48)	Jiroft (n=72)	p-value
Fatigue	50	35	60	0.22
Shortness of Breath	38	30	48	0.35
Cognitive Dysfunction (Brain Fog)	36	25	44	0.18
Headaches	28	27	38	0.45
Muscle/Joint Pain	30	26	40	0.60
Chest Pain	18	10	20	0.25
Loss of Taste/Smell	15	18	16	0.50
Sleep Disturbances	25	20	30	0.70
Heart Palpitations	12	14	20	0.40
Mental Health Challenges	23	18	28	0.65

the second common symptom, with Jiroft having the highest count (48), Khoy (38), and Bushehr (30). About Cognitive Dysfunction (Brain Fog): Jiroft again leads (44), followed by Khoy (36), and Bushehr (25). Headaches, muscle/joint pain, and mental health challenges also have notable counts. Neither the overall comparisons among all cities nor the pairwise comparisons showed any statistically significant differences for the symptoms.

Table 4 shows the context of healthcare access, with proportions of participants who primarily access healthcare in their respective cities, those with health insurance, and those that reported experiencing a financial burden due to healthcare costs. The majority of participants in all three cities report primary access to healthcare in their own city. Bushehr reports the highest proportion (290 - 300), suggesting well-established local care provision. Bushehr shows a notably higher proportion of participants with health insurance (260-300) compared to Khoy (220-300) and Jiroft (180 - 300). Jiroft reported the highest proportion reporting

TABLE 4.

Healthcare Access & Socioeconomic Factors for Participants.

Factor	Khoy	Bushehr	Jiroft
Primary Access to Health-care Location	270-300	290-300	280-300
Proportion of Participants with Health Insurance	220-300	260-300	180-300
Proportion of Participants reporting the financial burden of healthcare	150-300	80-300	180-300

a financial burden from healthcare (180 - 300), closely matched by Khoy (150 - 300). Bushehr reported a lower financial burden (80 - 300).

DISCUSSION

The findings of this study shed light on the heterogeneous burden of Long COVID across three major Iranian cities—Bushehr, Khoy, and Jiroft—highlighting the diverse and multifaceted nature of this condition in an understudied region. The prevalence and patterns of Long COVID symptoms observed in this study align with global trends, yet they also reveal unique contextual factors that underscore the importance of localized research in low- and middle-income countries. By examining the demographic, clinical, and socioeconomic dimensions of Long COVID, this study contributes to a growing body of evidence that emphasizes the need for tailored interventions and policies to address the long-term consequences of COVID-19.

The study found that a significant proportion of participants experienced persistent symptoms for more than 12 weeks following acute COVID-19 infection, with fatigue, shortness of breath, and cognitive impairments such as brain fog being the most commonly reported. These findings are consistent with global reports, which have identified fatigue and cognitive dysfunction as hallmark features of Long COVID [Greenhalgh *et al.*, 2020, Carfi *et al.*, 2020, Dennis *et al.*, 2023]. However, the high prevalence of psychological symptoms, particularly anxiety and depression, in our study population underscores the mental health toll of the pandemic in Iran, where pre-existing stressors such as economic instability and limited access to mental health services may exacerbate these conditions. The persistence of musculoskeletal pain and cardiovascular symptoms, such as chest pain and palpitations, further highlights the systemic nature of Long COVID and its potential to impact multiple organ systems.

Our analysis identified several risk factors associated with Long COVID, including older age, female gender, and the presence of pre-existing conditions such as obesity, diabetes, and cardiovascular diseases. The association between female gender and increased Long COVID risk has also been noted in previous studies, which suggests that women may exhibit heightened immune responses

and stronger inflammatory reactions, making them more susceptible to post-viral syndromes like Long COVID [Sudre *et al.*, 2021, Taquet *et al.*, 2021]. These observations align with findings from high-income countries, suggesting that certain biological and physiological vulnerabilities may predispose individuals to prolonged symptoms [Yan *et al.*, 2021, DePace and Colombo *et al.*, 2022]. However, the study also revealed unique socioeconomic and environmental factors that contribute to the burden of Long COVID in Iran. For instance, participants with lower educational attainment and those living in densely populated urban areas reported higher rates of persistent symptoms, likely due to limited access to healthcare and increased exposure to environmental pollutants. These findings highlight the intersection of health disparities and Long COVID, emphasizing the need for targeted interventions that address both medical and social determinants of health.

While the symptomatology and risk factors observed in this study align with global trends, the prevalence of Long COVID in our sample appears to be higher than reported in some high-income countries [Taquet *et al.*, 2021, Li *et al.*, 2024, Petersen *et al.*, 2022]. This discrepancy may be attributed to differences in healthcare infrastructure, access to post-COVID care, and the overall burden of the pandemic in Iran. For example, the high prevalence of fatigue and cognitive impairments in our study population may reflect the cumulative impact of prolonged stress and resource constraints during the pandemic. Additionally, the lack of standardized diagnostic criteria for Long COVID and variations in study methodologies may contribute to differences in reported prevalence rates. Nevertheless, the consistency of certain symptoms, such as fatigue and brain fog, across diverse populations underscores the universal nature of Long COVID as a global health challenge.

The findings of this study have important implications for healthcare planning and resource allocation in Iran and other low- and middle-income countries. The high burden of Long COVID, coupled with the limited capacity of healthcare systems to address post-COVID care, underscores the urgent need for integrated approaches that prioritize rehabilitation and mental health services. Establishing specialized Long COVID clinics, as has

been done in some high-income countries, could provide a model for delivering comprehensive care to affected individuals. However, such initiatives must be adapted to the local context, taking into account resource constraints and cultural factors that may influence healthcare-seeking behavior.

The high prevalence of psychological symptoms in our study population highlights the mental health crisis exacerbated by the pandemic. Anxiety and depression were particularly common among participants who experienced severe acute COVID-19 infections or had pre-existing mental health conditions. These findings underscore the need for mental health services to be integrated into post-COVID care programs, with a focus on early intervention and community-based support. Given the stigma associated with mental health in many low- and middle-income countries, public health campaigns to raise awareness about the psychological impacts of Long COVID may also be necessary to encourage help-seeking behavior. The study revealed significant socioeconomic disparities in the burden of Long COVID, with individuals from lower socioeconomic backgrounds reporting higher rates of persistent symptoms. These disparities are likely driven by factors such as limited access to healthcare, occupational exposure, and living conditions that increase the risk of infection and complicate recovery. Addressing these inequities will require multisectoral approaches that go beyond the healthcare system, including policies to improve housing, reduce occupational hazards, and expand social safety nets. Community-based interventions, such as mobile health clinics and telehealth services, may also play a critical role in reaching underserved populations.

Overall Summary and Implications and limitations:

Jiroft appears to have the highest burden of Long COVID within the study population, with a high prevalence rate, a higher presence of risk factors, the highest reporting of most symptoms, and also the most vulnerability with regard to financial burdens of healthcare, and lower levels of health insurance

coverage. This strongly suggests targeted interventions are needed in Jiroft. Khoy exhibits a concerning prevalence of Long COVID, with a relatively high number of risk factors and reported symptoms. Further investigation is required in Khoy to determine the specific drivers of Long COVID within the study population. Bushehr shows the lowest Long COVID prevalence within the study population, and lower reported rates of symptoms and risk factors among participants with health insurance and more access to local care; however, targeted support is still warranted, given that the study population still experienced Long COVID.

While this study provides valuable insights into the burden of Long COVID in Iran, several limitations must be acknowledged. The cross-sectional design limits our ability to establish causal relationships or track the trajectory of symptoms over time. Additionally, the reliance on self-reported data may introduce recall bias, particularly for participants who experienced mild or moderate acute infections. Future longitudinal studies are needed to better understand the natural history of Long COVID and identify predictors of recovery or chronicity. Furthermore, qualitative research could provide deeper insights into the lived experiences of individuals with Long COVID, informing the development of patient-centered interventions.

CONCLUSION

This study highlights the heterogeneous burden of Long COVID in three Iranian cities, emphasizing the complex interplay of biological, psychological, and social factors that shape its manifestation and impact. The findings underscore the need for a comprehensive and inclusive approach to addressing Long COVID, one that integrates medical care, mental health support, and social interventions to reduce disparities and improve outcomes. As the world continues to grapple with the enduring legacy of the pandemic, studies like this are essential for informing global and local strategies to mitigate the long-term consequences of COVID-19 and build more resilient healthcare systems.

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Ethical permission

Ethical approval was obtained from the Ethics Committee of Khoy University of Medical Sciences under the ethics code IR.KHOY.REC.1402.049.

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CONTENTS

4. **MOHAMMAD I., BARI M.N., ANSARI M.R., KHAN M.S., MOHAMMAD A.**
PATHOGENIC RESPONSE MECHANISMS TO HOST AND THERAPEUTIC STRESS: CHALLENGES IN ADVANCED MEDICAL MICROBIOLOGY
14. **MAKLETSOVA M.G., ZELENKOVA G.A., ZELENKOV A.P., USTYANTSEV D.A., VAKULENKO M.YU.**
POLYAMINES - FACTORS OF AGING AND LONGEVITY REGULATION. MINI-REVIEW.
31. **DEDIĆ L., BANJARI I., IMŠIROVIĆ DEDIĆ M., FERENAC KIŠ M., BARJAKTAROVIĆ-LABOVIĆ S.**
IS ALPHA LIPOIC ACID USEFUL IN OBESITY TREATMENT? A NARRATIVE REVIEW OF CLINICAL EVIDENCE
39. **SUKKAR S.R.I.**
PHYTOTOXINS IN FORENSIC MEDICINE AND INVESTIGATIONS: AN OUTLOOK TOWARDS THE INCREASING RELEVANCE
47. **MOFTAKHAR F., NEJADRASOLI M., BEHAEN K., GHOMEISHI A., FARHADI E., SAVAIE M.**
THE EFFECT OF SINGLE DOSE VITAMIN D3 INTRAMUSCULAR INJECTION DURING INTENSIVE CARE UNIT ON RENAL FUNCTION IN PATIENTS WITH TRAUMATIC INJURIES: A DOUBLE-BLINDED, RANDOMIZED, AND CONTROL TRIAL STUDY
54. **MOUSAVI M.J, AMIRZARGAR S., AREFINIA N., AJEL M., ARYAMAND S., BEHBOUDI E.**
UNVEILING THE HETEROGENEOUS BURDEN OF LONG COVID IN THREE IRANIAN CITIES
62. **ALSANOUSI N**
PHYTOCOMPOUNDS AS ANTIDIABETIC AND HEPATOPROTECTIVE AGENTS: THE PROMISING POTENTIALS OF ACACIA ARABICA (LAM.) WILDD FLORAL METHANOLIC EXTRACT
70. **DUNDOVIĆ M., FERENAC KIŠ M., MARCIJUŠ L., KLAPEC T., BANJARI I.**
INFLUENCE OF DIETARY IODINE ON SEMEN QUALITY PARAMETERS IN GENERAL MALE POPULATION: A PILOT STUDY
77. **IBRAHIM F.M., IBRAFIM M.M., SARDASHTI S.**
THE EVALUTAION OF CHAMOMILE AND TURMERIC ETHANOL EXTARCT PILL INTERVENTION IN COMPARISION WITH MEFNAMIC ACID ON THE SEVERITY OF PRIMARY DYSMENORREHA IN 18-21 YEARS OLD SINGLE STUDENTS
84. **PETROV YE.YE., KAZAKOV YU. M., BURMAK YU. H., IVANYTSKA T. A., CHEKALINA N. I., TRYBRAT T. A.**
COMPARATIVE CHARACTERISTICS OF SOME HOMEOSTASIS INDICES IN PATIENTS WITH CHRONIC COR PULMONALE IN DECOMPENSATION STAGE AND IN CONDITIONS OF ITS COMORBIDITY WITH STABLE CORONARY HEART DISEASE
91. **MUSTAFA M.O., IISA M.A., ABU BAKR I.M., KARRAR ALSHARIF M.H., ADAM A.H.**
THE DIFFERENCE IN PERCEPTION OF THE STUDENTS IN ANATOMY USING PROBLEM-BASED LEARNING AND LECTURES IN THE FACULTY OF MEDICINE, UNIVERSITY OF GADARIF.
97. **WINOTO S., HABAR T.R., HENDARTO J., KUSUMA M.I., PRIHANTONO P., MARIANA N., NURMANTU F., AHMADWIRAWAN A., SULMIATI S., FARUK M**
COMPARISON OF POST-DEFINITIVE-SURGERY COMPLICATIONS BETWEEN PATIENTS WITH HIGH AND LOW ANORECTAL MALFORMATIONS IN MAKASSAR, INDONESIA
104. **SHALCHI OGHLI S., SADEGHI R., OMRANIPOUR R., RAHIMI FOROUSHANI A., ASHOORKHANI M., TEDADI Y.**
EFFECTIVENESS OF TWO VIRTUAL PROGRAMS ON PERCEIVED STRESS, STRESS COPING, AND LIFE SATISFACTION AMONG WOMEN WITH BREAST CANCER: PROTOCOL FOR A RANDOMIZED CONTROLLED TRIAL
116. **KURNIAWATI E.M., VETERINI V, AZINAR A.D., PARATON H., HARDIANTO G., SETYOHADI T.H., RAHMAWATI N.A.**
CLINICAL EXPERIENCES OF UTERINE PROLAPSE OCCURRING DURING PREGNANCY IN TWO CASE REPORTS



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Armen A. **MURADYAN**

Address for correspondence:

Yerevan State Medical University
2 Koryun Street, Yerevan 0025,
Republic of Armenia

Phones:

(+37410) 582532 YSMU

(+37493 588697 Editor-in-Chief

Fax: (+37410) 582532

E-mail: namj.ysmu@gmail.com, ysmiu@mail.ru

URL: <http://www.ysmu.am>

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E-mail: monoprint1@mail.ru

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