

Territorial-Geographical Aspects, Pharmaco-Epidemiology and Prophylactic Characteristics of the Origin, Clinical Course and Complications of Comorbidity in the Geront Population (Literature Review)

Mamasoliev N. S.¹, Sirojiddinov K. B.², Mamasolieva Z. N.³, Nishonova N. A.⁴, Botirov J. A.⁵

¹Head of the Department of Cardiology, Doctor of Medical Sciences, Professor, Therapy and Emergency Medical Care of the Faculty of Advanced Training of Physicians, Andijan State Medical Institute, Andijan, Uzbekistan

²Department Applicant Faculty of Cardiology, Therapy and Emergency Medical Care of the Faculty of Advanced Training of Physicians, Andijan, Uzbekistan

³Doctor of Medical Sciences, Associate Professor, Department of Ophthalmology, Andijan, Uzbekistan

⁴Candidate of Medical Sciences, Associate Professor of the Department of Hospital Therapy and Endocrinology, Andijan, Uzbekistan

⁵Doctor of Medical Sciences, Associate Professor, Department of Surgical Diseases, Andijan, Uzbekistan

Abstract The authors have analyzed the origin, clinical course and complications of comorbidity in the geront population, regional-geographical aspects, pharmaco-epidemiological and preventive features, showing the relevance and necessity of the topic. In conclusion, it is generally concluded in most studies that drugs may increase the risk of fatal complications or toxicity in the geront population with iatrogenic multimorbidity syndrome. Gerontal patients always need "majority" supervision by relatives or medical personnel, especially in the case of comorbid diseases. This requires the improvement of the epidemiological, preventive and pharmacoepidemiological monitoring system in the geront population.

Keywords Epidemiological, Preventive and pharmacoepidemiological monitoring comorbidity, Population in geront esh, Drug iatrogenic

1. Introduction

It is worth noting that the influence of risk factors on the origin and development of comorbidity is more evident from the literature review. Diagnostic, screening - clinical pharmaco-epidemiological characteristics and preventive bases of comorbidity in geronts are mainly highlighted in clinical studies. It can be said that in the geront population, regionally and geographically, the prevalence of comorbidity is underestimated in routine clinical practice. Based on this, it can be assumed: the true prevalence of comorbidity (which is determined only in epidemiological studies) is higher than the generally accepted indicator.

Klip I.T. et al. (2013) studied the comorbidity of iron deficiency in chronic heart failure in 1506 individuals from Poland, Spain and the Netherlands. Such comorbidity was found in 50% of clients. The prognostic value of iron deficiency has been confirmed. In the presence of this factor,

the frequency of occurrence of "endpoints" caused by heart failure is doubled [23].

Jacob C. et al. (2019) studied 2,223 chronic heart failure patients in a retrospective cohort study in Austria. End points (death, heart transplant) combined with anemia comorbidity in chronic heart failure were detected in 62% of patients, in cases of anemia - 37% frequency [21].

In comorbidity, the issue of pharmacotherapy has a special place. In order to coordinate and secure therapy in the geront population, several algorithms for reducing the risk of polypharmacy have been developed and recommended for practice by researchers and scientific societies abroad and in Russia [15,29].

In order to prevent the risk of polypharmacy in the geront population, it is recommended to use the following questionnaires and algorithms: Prescription optimization method [13], Structured history taking of medication use questionnaire [14], " Palliative approach to solving the problem is polypharmacy in elderly patients" [8], scale ASV [Anticholinergic Cognitive Burden] [31], Medication Appropriateness Index [18], AGS [2] and START/STOPP

criteria [28].

Evidence suggests that most researchers in the geront population should always consider nonpharmacologic treatment first.

Even the study of Turnheim K. (2004) became known to us, in which the author asked gerontological and geront ages - is it necessary to use a pharmacological drug at all or is there a need for it? - the question is put crosswise [34].

Various system diseases contribute to comorbidity characteristically and differentially, in which increasing age is different and takes the leading place. Yardaniar A. *et al.* According to (2000), polypharmacy / polypharmacotherapy can be one of the factors that worsens the course of diseases in the gerontological and geront age population, in particular, the course of comorbid diseases [35].

Benjamin E.J. *et al.* (2019) advocate the principle of "a pill for every ill" for geront patients, strictly monitoring the treatment process with a multidisciplinary (team) approach, adding over-the-counter drugs and biologically active supplements, and limiting the number of doctors who prescribe drugs confirmed that it is appropriate to follow the rules as much as possible [6].

The question of reducing the risk of pharmacotherapy in the gerontological age population, mainly in clients with a comorbid background, Steenman M. *et al.* [33], Curties A.B. *et al.* [11], Meschiari C.A. *et al.* [27], Dee P.A. *et al.* [12], Burstein B. *et al.* [9] and Khan M.A. *et al.* It was also raised by foreign researchers such as [22] and made separate recommendations in this regard. For example, the reference to international clinical recommendations not to be used as a "Chinese wall" in the geront population comes from them.

In addition, the mentioned sources give clear conclusions on reducing the risk of pharmacotherapy against the background of cardiocomorbidity in the gerontological and geront population: 1) the risk of comorbidity in CKD after 60 years - 77.2% (in men) and 78.2% (in women), from 80 years - 89.3% and increases to 91.8%; 2) geronts dramatically increase the risk of heart failure, arrhythmias (mainly atrial fibrillation) and arterial hypertension; 3) against the background of cardio comorbidity, the main pathogenetic factors causing and aggravating HD (proinflammatory markers and oxidative stress level, apoptosis, cardiomyocyte aging process, degenerative processes, interleukin-6, α -tumor necrosis factor, S-reactive protein) are aggravated, firstly, cardiac pathologies, for example, increases the frequency of CHD and secondly their risk when the geront gets older.

As a result of comorbidity in CD (for example, atherosclerotic diseases), there are diseases noted with high frequency in the geront population - AG (85.6% and 80.0% are observed in women and men), CD (15,000 to 100,000 people), myocardial infarction (from 11.5% and 4.2% of men and women), ventricular fibrillation (10.0%) and strokes (up to 23.5%) are counted [9,22,25,26].

Another factor that should be considered or considered important in the treatment of comorbid conditions in the geront population is that this population is often shown in studies to have a relatively low level of fear of drugs (drug

habituation) and adherence to pharmacotherapy. Haynes RB, McDonald H. *et al.* (2002), Bloom B.S. (2001) and Benner J.S. *et al.* (2002) according to the presented scientific results, for example, more than 50% of the elderly of gerontological -geront age do not adhere to prescribed pharmacotherapy for chronic (comorbid) diseases [5,7,19].

Kronish I.M., Diefenbach MA, Edmondson DE. *et al.* (2012) convincingly confirm that one of the main reasons for the fear or anxiety of drug addiction (DD) in geront patients is the formation of a completely wrong view of the presence of certain problems of the drug being used. In addition, gerontological age and gerontology-related memory decline, cognitive impairment, fear and hearing loss, and of course health comorbidities and reduced obligations to respond to medications [24].

Anderson L.J. is one of the reasons why comorbid diseases are increasing in the geront population and in the elderly in general. *et al.* [4] and Sergi G. *et al.* According to [32], it is a complex pharmacotherapy regimen or Greeberg R.N. [17] and Claxton A.J. According to scientific conclusions presented by *et al.* [10], the percentage of pharmacotherapeutic obligation fulfillment and related problems of geriatric-geront comorbidities increase as the frequency of taking DD increases: when the drug is taken once a day - 73-79%, twice when drinking - 69-70%, when drinking three times - 52-65%, and when drinking 4 times - 42-51%.

Confirmation of negative effects as a risk factor for comorbidity (total of 15 cases) as well as polypharmacotherapy was reliably reported and confirmed by the following researchers: Alosco M.L. *et al.* [1], Heringer C. *et al.* [20], Al Shaikh S. *et al.* [3], Rohde D. *et al.* [30] and Gelled W.F. *et al.* [16].

2. Summary

Therefore, it is generally concluded in most studies that drugs may increase the risk of fatal complications or toxicity in the geront population with iatrogenic multimorbidity syndrome. Geront patients always need "majority" supervision by relatives or medical personnel, especially in the case of comorbid diseases. This requires the improvement of the epidemiological, preventive and pharmacoepidemiological monitoring system in the geront population.

REFERENCES

- [1] Ibadova M.Yu. Pathogenetic significance of metabolic syndrome in the formation of multimorbid diseases // Abstract of the dissertation...doctor. Philosophy (PhD) in Medical Sciences. -2024. -C.
- [2] 2019. American Geriatrics Society Beers Criteria Update Expert Panel American Geriatrics Society 2019 Updated AGS Beers Criteria for Potentially Inappropriate Medication Use in Older Adults // J. AM. Geriatr. Soc. -2019. -Vol. 67. - № 4. - P. 675-693. DOI: 10.1111/igs.15767.
- [3] Al ShaiKh S., Quiann T., Dunn W., *et al.* Preventive factor of

non-adherence to secondary preventative medication after stroke or transient ischemic attack: A systematic review and meta-analyses // *Eur. Stroke J.* -2016. -Vol.1. -N2. -P66-72. DOI: 10.1177/2396 987316647187.

- [4] Anderson L.J., Nuckola T.K., Coles C. et al. A systematic overview of systematic reviews evaluating medication adherence in interventions // *Am. J. Health syst. pharm.* - 2020 - Vol. 77. - N. 2. -P. 139-145. DOI: 10.1093/ajhp/ztx284.
- [5] Banner J.S., Glynn R.J., Mogun H. Et al. Long-term persistence in use of statin therapy in elderly patients // *JAMA.* -2002. - Vol. 288. - № 4. - P. 456-460.
- [6] Benjamin E.J., Muntner P., Alonso A., et al. American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. Heart Disease and Stroke Statistics-2019 Update: A Report from the American Heart Association // *Circulation/CiR-*0000000000000659. PMID: 30700139.
- [7] Bloom B.S. Daily regimen and compliance with treatment // *BMJ.*2001-Vol.328.-Issue 7314. -P. 645-646.
- [8] Boustani M., Campbell N., Munger S. Et al. Impact of anticholinergic on the aging brain: a review and practical application // *Aging Health.* - 2008. - Vol. 4. - N3 -P. 312-318. DOI: 10.2217/1745509X.4.3.311.
- [9] Burstein B., Nattel S. Atrial Fibrosis: mechanisms and clinical relevance in atrial fibrillation // *J. Am. Coll. Cardiol.* 2008. - Vol. 51. - P. 803-807. DOI: 1.1016/J. jacc. -2007.09. 064.
- [10] Claxton A.J., Cramer J., Pierce C. A systematic reviews of the associations between dose regimens and medication compliance // *Clin. Ther.* -2001. - Vol. 23. -N 8. -P. 1207-1309.
- [11] Curties A.B., Karki R., Hattoum A., Sharma V.C., Arrhythmias in Patents 80 years of Age: Pathophysiology, Management, and Outcomes // *J. Am. Coll. Cardiol.* -2018. - Vol. 71. - N. 18. -P. 2042-2045. Doi: 10.1016/J. jacc. 2018.03.019. PMID: 29724357. PMID: PMC 5942187.
- [12] Di P.A., Caruso E., Costanzo L., Guccione P. A novel Ry R2 mutation in a 2-year old baby presenting with atrial fibrillation, atrial flutter, and atrial ectopic tachycardia // *Heart. Rhythm.* - 2014. - Vol. 11. -P. 1481-1482. Doi: 10.1016/j. rhythm. 2014. 04. 037.
- [13] Drenth-van Maanen A.C., van Marum R.J., Knd W., Prescription optimization method for improving prescribing in elderly patients receiving polypharmacy: results of application to case histories by general practitioners // *Drugs Aging.* -2009. - Vol. 26. - N8. - P. 688-700.
- [14] Garfunkel D., Mangin D., Feasibility study of a systematic approach for discontinuation of multiple medications in older adults: addressing polypharmacy // *Arch. Inter. Med.* -2010. - Vol.170. -N18. - P. 1649-1653. DOI: 1.1001/archinternmed. 2010.355.
- [15] Garfunkel D., Zur-Gii S., Ben-Iaral J. The war against polypharmacy: a new cost-effective geriatric-palliative approach for improving drug therapy in disabled elderly people // *Iar. Med. Assoc. J.* - 2007. - Vol. 9. -N. 6. - P. 431-432.
- [16] Gelled W.F., Grenard J.L., Marcum Z.A., A systematic review of barriers to medication adherence in the elderly: looking beyond cost and regimen complexity // *Am. J Geriatr Pharmacother.* - 2011. - Feb. -Vol. 9. - N1. -P. 11-21. DOI: 10.1016/j.am. jopharm.-2011.02. 004.
- P MID; 21459305. PMID: PMC3084587.
- [17] Greenberg R.N., Overview of patient compliance with medication dosing: a literature review // *Clin. Ther.* - 1984. - Vol. 6. - N. 5. - P. 593-597.
- [18] Hanlon J.T., Schmader K.E., Samsa G.P. A method for assessing drug therapy appropriateness // *J. Clin. Epidemiol.* - 1992. - Vol. 95. - P. 1045-1049.
- [19] Haynes R.B., Mc Donald H., Garg A, X. Montague P. Interventions for helping patients to follow prescriptions for medication s // *Co-Cochrane Database Syst. Rev.* 2002 - № 2. - P. - CD000011.
- [20] Herringer C., Klotz V. Drug metabolism and drug interactions in the elderly // *Best Pract. Res. Clin. gastroenterol.* - 2001. -Vol. 15. - N. 6 -P.898-915.
- [21] Jacob C., Altevors J., Barck I. Et al. Retrospective analysis into differences in heart failure patients with and without iron deficiency or anemia / *ESC Heart Fail.* -2019; 6(4): 840-52: DOI: 10.1002/ehf2.12485.
- [22] Khon M.A., Hashim M.J., Mustafa H. et al. Global Epidemiology of ischemic Heart disease: Results from the Global Burden of disease study // *Curens.* 2020.-Vol.12.-N7. e9348. Published 2020 Jul 23. DOI: 10.7759/curens. 9349.
- [23] Klip I.T., Comin-Colet J., Voors A.A., Iron deficiency in chronic heart failure: on international pooled analysis // *Am Heart J.* -2013: 165-375-80.
- [24] Kronish I.M., Dicfenbach M.A., Edmondson D. E et al. Key barriers to medication adherence in survivors of strokes and transient ischemic attacks // *J. Gen / Intern. Med.* -2013. - Vol. 28. -N5. - P. 674-681. DOI:10.1093/ajhp/zxz284.
- [25] Lam C.S., Kienstra M., Tay W.T. et al. Atrial fibrillation in heart failure with preserved ejection fraction: association with exercise capacity, left ventricular filling pressures, natriuretic peptides left atrial volume // *JACC Heart Fail.* - 2017. - Vol. 5 - P. 93-95. DOI: 10.1016/j.jchf.2016.10.005.
- [26] Ling L.H., Kistler P.M., Ellims A.H. et al. Diffuse ventricular fibrosis in atrial fibrillation: noninvasive evaluation and relationship with aging and autonomic dysfunction // *J. Am. Coll. Cardiol.* - 2012. - Vol. 6. 9. -2403-2406.
- [27] Meschiaro C.A., Ero O.K., Pan H. et al. The impact of aging on cardiac extracellular matrix // *Geroscience.* -2017. -Vol. 39. - P. 7-15.
- [28] O'Mahony D., O'Sullivan D., Byrne S., et al. STOPP/START criteria for lished correction appears in *Age Ageing.* - 2018. - Vol. 47. -N3. -P.4 884] // *Age Ageing.* -2015. - Vol. 44 - № 2. -P. 214-217. DOI: 10.1093/ageing/afu 145.
- [29] Poudel A., Ballokarova A., Hubbard R.E. Algorithm of medication review in frail older people: Focus on minimizing the use of high-risk medications // *Geriatr. Gerontol. Int.* -2016. - Vol. 16. - N. 9. - P. 104-1011. DOI: 10.1111/ggi.12589.
- [30] Rohde D., Gaynor E., Large M. Et al. Cognitive impairment and medication adherence post-stroke: A five -year follow up of the ASPIRE -S cohort // *PhoS One.* 2019. - Vol. 14. - N. 10. -P. e0223997.
- [31] Rowe T.A., Juthani-Menta M. Urinary tract infection in older adults // *Aging health.* - 2023. - 9(5): 526. DOI: 10.2217/ane.

13-38.

PMID: 28510085. PMCID: PMC5418492.

- [32] Seryi C., De Rui M., Sarti S., Manzato E. Polypharmacy in the elderly: can comprehensive geriatric assessment reduce inappropriate medication use? // *Drugs Aging*. -2011. -Vol. 28 - № 7. - P. 511-517.
- [33] Steenman M., Lande G. Cardiac aging and heart disease in humans / *Biophys. - Rev.* 2017. - Vol. 9. - N2. -P. 132-135. DOI: 10.1007/s 12551-017-0255-8. Epub 2017. Mar 20.
- [34] Turnhelm K. Drug therapy in the elderly / *Exp. Gerontol.* -2004. - Vol. 39. - № 11-12. - P. 1731-1735. DOI: 10.1016/J.exger.2004.05.011. PMID: 15582389.
- [35] Vardanyar A., Newman A.B. The burden of cardiovascular disease in the elderly: morbidity, mortality, and costs // *Clin. Greatr. Med.* - 2000. -Vol. 25 - N4. - P. 562.-vit. Doi: 10.1016/j.eger.2009.07.007.