HORMONAL AND GENETIC CHARACTERISTICS OF SEX HORMONE METABOLISM IN NON-ALCOHOLIC FATTY LIVER DISEASE AMONG WOMEN OF REPRODUCTIVE AGE

Yunusova Dilfuza Jamolidin qizi

Assistant Lecturer, Department of Normal Physiology Andijan State Medical Institute

Ravzatov Jasurbek Baxromovich

PhD, Associate Professor, Department of Family Physician Training Andijan State Medical Institute

Abstract

Non-alcoholic fatty liver disease (NAFLD) is one of the most pressing issues in modern hepatology, endocrinology, and metabolic medicine. Its development is closely associated with insulin resistance, visceral obesity, dyslipidemia, chronic low-grade inflammation, oxidative stress, and fibrotic processes. In recent years, international hepatology literature has increasingly referred to this condition as metabolic dysfunction-associated steatotic liver disease (MASLD). According to the 2024 clinical guidelines of the European associations for liver, diabetes, and obesity research, MASLD is characterized by hepatic steatosis accompanied by at least one cardiometabolic risk factor. This study focuses on the hormonal and genetic features of sex hormone metabolism in women of reproductive age with non-alcoholic fatty liver disease, highlighting the role of endocrine and genetic factors in the pathogenesis and progression of the disease.

Keywords

non-alcoholic fatty liver disease (NAFLD), reproductive age, estrogens, androgens, SHBG, CYP19A1, UGT2B15, UGT2B17, polycystic ovary syndrome (PCOS), insulin resistance.

REPRODUKTIV YOSHDAGI AYOLLARDA NOALKOGOL YOG‘LI JIGAR KASALLIGIDA JINSIY GORMONLAR METABOLIZMINING GORMONAL-GENETIK XUSUSIYATLARI

Yunusova Dilfuza Jamolidin qizi

Andijon davlat tibbiyot instituti Normal fiziologiya kafedrasi assistenti

Ravzatov Jasurbek Baxromovich

Andijon davlat tibbiyot instituti Oilaviy shifokorlar tayyorlash kafedrasi PhD, dotsenti

Annotatsiya. Noalkogol yog‘li jigar kasalligi zamonaviy gepatologiya, endokrinologiya va metabolik tibbiyotning dolzarb muammolaridan biri bo‘lib, uning rivojlanishida insulinrezistentlik, visseral semizlik, dislipidemiya, surunkali past darajadagi yallig‘lanish, oksidlovchi stress va fibrozlanish jarayonlari muhim o‘rin tutadi. So‘nggi yillarda xalqaro gepatologik adabiyotlarda ushbu kasallik metabolik disfunksiya bilan bog‘liq steatotik jigar kasalligi sifatida ham talqin qilinmoqda. EASL–EASD–EASO 2024-yilgi klinik tavsiyalarida metabolik disfunksiya bilan bog‘liq steatotik jigar kasalligi jigar steatozi va kamida bitta kardiometabolik xavf omili mavjudligi bilan tavsiflanishi ko‘rsatilgan [1; 492–495-b.].

Kalit so‘zlar: *noalkogol yog‘li jigar kasalligi, reproduktiv yosh, estrogenlar, androgenlar, SHBG, CYP19A1, UGT2B15, UGT2B17, tuxumdonlar polikistoz sindromi, insulinrezistentlik.*

Noalkogol yog‘li jigar kasalligi oddiy steatozdan boshlab steatogepatit, jigar fibrozi, sirroz va gepatotsellyulyar karsinomagacha rivojlanishi mumkin bo‘lgan keng klinik spektrga ega. AASLD 2023-yilgi amaliy qo‘llanmasida noalkogol yog‘li jigar kasalligi nafaqat gepatologik, balki kardiometabolik xavf bilan bog‘liq tizimli patologiya sifatida baholanishi zarurligi ta’kidlangan [2; 1797–1805-b.]. Ushbu holat kasallikni erta

aniqlash, xavf guruhlarini ajratish va fibrozlanish ehtimolini noinvaziv usullar bilan baholash zarurligini ko‘rsatadi.

Reproduktiv yoshdagi ayollarda kasallikning o‘ziga xosligi shundaki, bu davrda estrogenlar, progesteron, androgenlar va ularni tashuvchi oqsillar lipid almashinuvi, glyukoza homeostazi, visseral yog‘ to‘planishi, yallig‘lanish javobi va jigar to‘qimasidagi metabolik jarayonlarga bevosita ta’sir ko‘rsatadi. Estrogenlar odatda insulin sezgirligini qo‘llab-quvvatlovchi va jigar lipid almashinuvini muvozanatlashtiruvchi himoyalovchi omil sifatida qaraladi. Biroq giperandrogenizm, insulinrezistentlik, abdominal semizlik va SHBG darajasining pasayishi fonida ushbu himoya mexanizmlari zaiflashadi [3].

Tuxumdonlar polikistoz sindromi reproduktiv yoshdagi ayollarda noalkogol yog‘li jigar kasalligi bilan eng ko‘p bog‘liq bo‘lgan endokrin-metabolik holatlardan biridir. Adabiyotlarda tuxumdonlar polikistoz sindromi bo‘lgan ayollarda jigar yog‘lanishi umumiy ayollar populyatsiyasiga nisbatan ko‘proq uchrashi, bunda insulinrezistentlik, giperandrogenemiya va qorin sohasi semizligi muhim ahamiyatga ega ekani qayd etilgan [4]. Shu sababli reproduktiv yoshdagi ayollarda noalkogol yog‘li jigar kasalligini faqat tana vazni, transaminazalar yoki ultratovush tekshiruvi bilan baholash yetarli emas; bunda gormonal va genetik markerlarni ham kompleks o‘rganish zarur.

Tadqiqot maqsadi

Reproduktiv yoshdagi ayollarda noalkogol yog‘li jigar kasalligida jinsiy gormonlar metabolizmining gormonal-genetik xususiyatlarini o‘rganish, SHBG, CYP19A1, UGT2B15 va UGT2B17 genlari bilan klinik-metabolik, biokimyoviy va instrumental ko‘rsatkichlar o‘rtasidagi ehtimoliy bog‘liqlikni ilmiy asoslash.

Asosiy qism

Noalkogol yog‘li jigar kasalligi patogenezida insulinrezistentlik markaziy bo‘g‘in hisoblanadi. Insulin ta’sirining susayishi yog‘ to‘qimasidan erkin yog‘ kislotalari

oqimini kuchaytiradi, gepatotsitlarda triglitseridlar to‘planishini oshiradi, de novo lipogenezni faollashtiradi, mitoxondrial β-oksidlanishni izdan chiqaradi va oksidlovchi stressni kuchaytiradi. Buning natijasida gepatotsit shikastlanishi, yallig‘lanish mediatorlari ko‘payishi va fibrogenez jarayonlari faollashadi [2; 1801–1810-b.].

Ayollarda jinsiy gormonlar jigar metabolizmini muhim darajada modulyatsiya qiladi. Estrogenlar lipidlar almashinuvi, glyukoza homeostazi, mitoxondrial faoliyat va yallig‘lanish javobini tartibga solishda ishtirok etadi. Estrogen signalining susayishi yoki androgenlar biologik faolligining ortishi jigarda lipotoksiklik, insulinrezistentlik va steatoz rivojlanishiga moyillikni kuchaytirishi mumkin [3]. Shu sababli reproduktiv yoshdagi ayollarda noalkogol yog‘li jigar kasalligi ko‘pincha endokrin-metabolik fenotip sifatida namoyon bo‘ladi.

Jinsiy gormonlarni bog‘lovchi globulin jigar tomonidan sintez qilinadigan oqsil bo‘lib, qonda testosteron va estradiolning erkin fraksiyasini tartibga soladi. SHBG darajasining pasayishi erkin androgenlar ulushining ortishi, insulinrezistentlik va jigar yog‘lanishi bilan bog‘liq bo‘lishi mumkin. Di Stasi va hammualliflar tomonidan o‘tkazilgan tadqiqotda SHBG darajasining 33,4 nmol/l dan past bo‘lishi ayollarda noalkogol yog‘li jigar kasalligi xavfi bilan bog‘liq marker sifatida baholangan [5]. Ushbu ma’lumot SHBGni reproduktiv yoshdagi ayollarda gormonal-metabolik xavfni baholashda muhim amaliy ko‘rsatkich sifatida o‘rganish zarurligini ko‘rsatadi.

CYP19A1 geni aromataza fermentini kodlaydi. Aromataza androgenlarni estrogenlarga aylantirishda ishtirok etadi va ayol organizmida estrogen-androgen nisbatini saqlashda muhim rol o‘ynaydi. CYP19A1 polimorfizmlari tuxumdonlar polikistoz sindromi, giperandrogenizm va reproduktiv-endokrin buzilishlarga moyillik bilan bog‘liq bo‘lishi mumkin. Xing va hammualliflar tomonidan o‘tkazilgan meta-tahlilda CYP19A1, CYP17A1 va SHBG genlari polimorfizmlarining tuxumdonlar polikistoz sindromiga moyillikdagi o‘rni tahlil qilingan [6]. Garchi CYP19A1 genining

aynan noalkogol yog‘li jigar kasalligidagi mustaqil roli to‘liq isbotlanmagan bo‘lsa-da, uning jinsiy gormonlar metabolizmidagi vazifasi ushbu genni istiqbolli nomzod marker sifatida o‘rganishga asos beradi.

UGT2B15 va UGT2B17 genlari steroid gormonlar, xususan testosteron va dihidrotestosteron kabi androgenlarning glyukuronidlanishida ishtirok etuvchi fermentlarni kodlaydi. Bu fermentlar androgenlarning biologik faolligini pasaytirish va ularni organizmdan chiqarishda muhim ahamiyatga ega. UGT2B17 genining tabiiy yetishmovchiligi yoki deletsiya varianti androgen almashinuvi, jigar proteomi va metabolik yo‘llardagi o‘zgarishlar bilan bog‘liq bo‘lishi mumkin. 2025-yilda e’lon qilingan proteomik tadqiqotda UGT2B17 to‘liq yetishmovchiligi jigarda metabolik, stress va immun javob bilan bog‘liq oqsil profili o‘zgarishlari bilan kechishi ko‘rsatilgan [7].

Mazkur genlarning noalkogol yog‘li jigar kasalligida o‘rganilishi ayniqsa reproduktiv yoshdagi ayollar uchun muhimdir. Chunki ushbu guruhda jinsiy gormonlar metabolizmi, menstrual sikl xususiyatlari, tuxumdonlar polikistoz sindromi, giperandrogenizm va insulinrezistentlik bir-biri bilan uzviy bog‘langan holda kasallikning klinik kechishini belgilashi mumkin. O‘zbek populyatsiyasida SHBG, CYP19A1, UGT2B15 va UGT2B17 genlari polimorfizmlari bilan noalkogol yog‘li jigar kasalligi o‘rtasidagi bog‘liqlik yetarli darajada o‘rganilmagan. Bu esa mazkur yo‘nalishdagi tadqiqotning ilmiy yangiligi va amaliy ahamiyatini belgilaydi.

Xulosa

Reproduktiv yoshdagi ayollarda noalkogol yog‘li jigar kasalligi ko‘p omilli metabolik-endokrin patologiya bo‘lib, uning rivojlanishida insulinrezistentlik, abdominal semizlik va dislipidemiya bilan bir qatorda jinsiy gormonlar metabolizmi ham muhim ahamiyatga ega. Estrogen-androgen muvozanatining buzilishi, SHBG darajasining pasayishi, tuxumdonlar polikistoz sindromi hamda CYP19A1, UGT2B15

va UGT2B17 genlarining funksional xususiyatlari kasallikning shakllanishi va kechishiga ta’sir ko‘rsatishi mumkin. SHBG amaliy biomarker sifatida nisbatan ko‘proq ilmiy asoslangan bo‘lsa, CYP19A1, UGT2B15 va UGT2B17 genlari reproduktiv yoshdagi ayollarda noalkogol yog‘li jigar kasalligining gormonal-genetik mexanizmlarini chuqurroq o‘rganish uchun istiqbolli nomzod markerlar hisoblanadi. Ushbu markerlarni klinik, antropometrik, biokimyoviy va instrumental ko‘rsatkichlar bilan integratsiyalash kasallikni erta aniqlash, individual xavfni baholash va profilaktik yondashuvlarni takomillashtirishga xizmat qiladi.

Foydalanilgan adabiyotlar

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