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Antibiotic Resistance of *Acinetobacter baumannii* in Women with Polycystic Ovary Syndrome

Nawal B.Yazea[1*]; Dhuha M. Abbas[2]; Rand Moshtaq Talib[3]

Department of biology, College of Science, University of Al Mustansiriyah, Baghdad, Iraq
Correspondence*: Nawal B.Yazea[1*]

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Abstract: The common Gram-negative pathogenic bacterium *Acinetobacter baumannii* is can result in severe illnesses and is resistant to a variety of drugs.. Women who are of childbearing age are affected by polycystic ovary syndrome, which can present with a variety of symptoms. Insulin resistance is a result of hormonal and metabolic issues that affect women and can develop to type 2 diabetes. Since individuals with diabetes or insulin resistance are known to have compromised immune systems, the body becomes an ideal habitat for a variety of microorganisms, including *Acinetobacter baumannii*. Objective of this review is to demonstrate the antibiotic resistance of *acinetobacter baumannii* with polycystic ovary syndrome

***Keywords**: Acinetobacter baumannii, Polycystic Ovary Syndrome, Insulin Resistance, Diabetes Mellitus.*

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I. INTRODUCTION

One of the most prevalent multidrug-resistant bacteria (1) and a significant cause of nosocomial infections is Acinetobacter baumannii. The uncontrolled use of antibiotics is One of the primary reasons why multidrug-resistant A. baumannii infections are becoming more common. Drug resistance in A. baumannii is strong, especially when it comes to tigecycline and polymyxin, which are used as last resorts for strains of the bacteria that are very resistant to drugs. Patients with severe infections brought on by *A. baumannii*, which is widely resistant to antibiotics, have a dismal prognosis and a high death rate.(2), In hospital settings, *Acinetobacter baumannii* is a serious risk(3), particularly for seriously ill patients who need extended hospital stays. Because of its exceptional genetic plasticity, which enables it to quickly evolve resistance, especially in unfavourable environmental conditions, this disease is becoming more difficult to manage and avoid. Its reputation as a major public health concern has prompted efforts to find better infection control methods and innovative treatment alternatives. Notably, the antimicrobial medicines that are now on the market are becoming less effective with time.(4) Five to twenty percent of women of reproductive age suffer from polycystic ovarian syndrome (PCOS), a complex and multidimensional endocrine disorder (5). (6) The diagnostic criteria (7) state that the syndrome is linked to gynecological and hyperandrogenic traits as well as metabolic abnormalities such obesity, dyslipidemia, hyperinsulinemia, and insulin resistance (IR). Nonetheless, there is ongoing discussion over the correlations between these factors and the link between metabolic disorders and the hyperandrogenic state. The essential hormone insulin, which is generated by the beta cells of the pancreas, is essential for preserving glucose homeostasis and controlling a number of bodily metabolic functions. Given the rising incidence of insulin-related diseases including type 2 diabetes and metabolic syndrome, it is imperative to comprehend how insulin works and how insulin resistance develops(8). Insulin resistance happens when cells in the body lose their sensitivity to the actions of insulin, which makes it harder for the body to properly control glucose metabolism and other cellular functions. Therefore, to keep blood glucose levels within normal ranges, more insulin is required. Insulin resistance, a hallmark of type 2 diabetes mellitus, is also present in metabolic diseases such obesity, metabolic syndrome, and polycystic ovarian syndrome (PCOS).Reduced insulin sensitivity in tissues such as the liver, skeletal muscle, and adipose tissue causes cells to absorb glucose less efficiently, blood glucose levels to rise (hyperglycemia), and the pancreas to produce more insulin (hyperinsulinemia) (9).

II. EFFECT OF POLYCYSTIC OVARIAN SYNDROME ON INSULIN LEVEL IN WOMEN PCOS

Anovulation, infertility, obesity, insulin resistance, and polycystic ovaries are prominent symptoms of PCOS, a complex condition combining both endocrine and metabolic dysfunctions. Women may be predisposed to PCOS by a number of risk factors, such as food or lifestyle choices, environmental contaminants, obesity, neuroendocrine

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disorders, gut dysbiosis, and heredity. These factors may contribute to the development of metabolic syndrome by causing hyperinsulinemia, oxidative stress, hyperandrogenism, poor folliculogenesis, and irregular menstrual cycles The Rotterdam criteria (10) state that women with normal insulin sensitivity or minor insulin resistance are examples of non-classical PCOS phenotypes(11), In women with PCOS, have a hormonal imbalance in testosterone(12). excess testosterone encourages the buildup of belly fat, which worsens insulin resistance and causes compensatory hyperinsulinemia, which raises the production of ovarian testosterone even more(13). Thus, in order to improve metabolic comorbidities and reproductive outcomes in women with PCOS, therapy approaches concentrate on weight loss and reducing the detrimental metabolic consequences of abdominal obesity(14).

III. THE RELATIONSHIP BETWEEN INSULIN RESISTANCE, TYPE 2 DIABETES, IMMUNE REACTIONS AND INFLAMMATION

A complicated metabolic illness with sophisticated pathophysiological pathways, insulin resistance (IR) is widely acknowledged as a major etiological component in a number of diseases. Internal environmental elements that lead to pathological changes in the body, including inflammation, metabolism, and obesity, are intimately associated with the development of IR(15)(16). The pathogenesis of insulin resistance, obesity, and obesity-induced insulin resistance is significantly influenced by inflammation. Because inflammatory signals interfere with insulin signalling, chronic inflammation linked to obesity is implicated in the development of IR (14). Moreover, varying degrees of systemic and tissue-specific IR have been associated with differences in circulating immune cell populations and inflammatory markers. (17) (18).Numerous immune system changes are indicative of chronic inflammation linked to obesity and IR. For example, compared to lean people, obese people have higher amounts of inflammatory mediators such as IL-6 and TNF-a(19). Additionally, alterations in immunological populations, such as variations in lymphocyte subtypes, are associated with obesity and IR. These changes hinder pathogen-specific responses and raise the risk of infection(20). An increase in monocytes also contributes to chronic inflammation(21). Immune effector functions have also been observed to have altered; for instance, circulating monocytes in obese individuals take on a proinflammatory nature. This adaptation is characterised by increased surface expression of Toll-like receptors (TLRs) and chemokines, as well as increased TLR4-mediated IL-1β release, in comparison to those with a healthy body weight(22)(23). Type 2 diabetes (T2D) is a complicated disease that is primarily caused by hyperglycemia and peripheral and hepatic insulin resistance.(24). T2D is a rising worldwide health concern that affects more than 10% of Americans and presents with a range of comorbidities and inflammatory abnormalities. This dysregulated host response makes the host more vulnerable to infections from a variety of microbes. Chronic infections such foot ulcers and periodontitis can develop in people with type 2 diabetes as the disease worsens, which can result in more problems and opportunistic infections at other body locations.(25).

IV. GROWTH AND INFECTIONS OF *ACINETOBACTER BAUMANNII* IN DIABETIC PATIENTS

Impaired insulin signalling, a hallmark of diabetes mellitus (DM), is linked to an increased risk and intensity of infections. Bacterial infections can develop due to a number of diabetes-related problems, including hyperglycemia, innate immune cell malfunction, and infections with bacteria that are resistant to antibiotics. A defining feature of diabetes, hyperglycemia raises blood and tissue glucose levels, which gives a number of bacterial infections the perfect carbon source to grow and become more virulent. Chronic infections are known to be exacerbated by bacterial virulence mechanisms such tissue adhesion and biofilm development, which are encouraged by this elevated glucose level. Foot infections, which frequently feature biofilm-associated polymicrobial communities, are a significant source of morbidity in diabetics. Bacteria participate in intricate interspecies interactions within these biofilms, such as metabolic cross-feeding and the emergence of phenotypes more resistant to antibiotic treatment, that improve their growth and virulence. Moreover, diabetes-induced metabolic dysfunction compromises immune cell function, resulting in immunological suppression(26). Increased mortality from *Acinetobacter baumannii* (AB) complex infections is also linked to diabetes. The risk factors and the association between glycaemic indices and diabetes status and mortality in patients with carbapenem-resistant (CR) AB complex bacteremia were investigated in this study(27). In a different investigation, cytokine profiles and microbiome signatures were examined in serum samples from individuals in good health and those with type 2 diabetes (T2D), T2DP, or no periodontitis. Interestingly, 23% of people with T2D/T2DP had *Acinetobacter baumannii* in their serum. The levels of IL-1β, TNF-α, MCP-1, IL-6, IL-8, and IFN-γ were considerably greater in T2DP subjects who tested positive for AB. In individuals with type 2 diabetes, infection with the newly discovered pathogen *A. baumannii* reduces inflammation and raises the risk of comorbidities(25). Between January 1st, 2010, 428 adult patients with carbapenem-resistant *Acinetobacter baumannii* complex (CRAB) bacteremia were admitted to hospitals; the data of 317 of those individuals were available for analysis. With a death rate of 57.73%, the patients' demographic and clinical features were 66.1 ± 16.87 years. 146/317, or.06%, of the 317 patients had diabetes. The mean age of DM patients was 69.23 ± 12.88 years, and they had higher APACHE II scores (29.83 ± 7.82 vs. 27.1 ± 8.65, $p = 0.006$) and a higher mortality rate (64.38% vs. 52.05%, $p = 0.036$),Furthermore, compared to non-DM patients, a higher percentage of DM patients had cardiac disease, septic shock, and chronic kidney disease.(27).

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V. BACTERIAL RESISTANCE IN DIABETES PATIENTS AND INSULIN RESISTANCE

Acquired resistance to at least one agent in three or more antimicrobial categories characterises bacterial illnesses that are multidrug-resistant (MDR). These infections are become more prevalent and represent a serious risk to public health since they increase morbidity, mortality, medical expenses, and the need for antibiotics.(28)(29). The severity of MDR bacterial infections is influenced by a number of factors, such as those observed in diabetic foot ulcers (DFUs), such as longer hospital admissions, higher treatment expenses, higher mortality rates, and an increased chance of lower extremity amputation(30). Diabetes is acknowledged as a significant risk factor for certain intracellular bacterial infections, despite the fact that research on the dysregulated immunological pathways that impede host-pathogen interactions is still in its early stages. Diabetes is characterized by chronic low-grade inflammation due to the elevated synthesis of advanced glycation end products and the activation of pro-inflammatory mediators. The chronic inflammatory processes linked to diabetes are made worse by increased oxidative stress. An intracellular milieu that is favourable to pathogen replication is produced by neutrophils' and macrophages' diminished phagocytic and antibacterial activity. Changes in glucose metabolism and oxidative stress may have a direct impact on this impairment in phagocytic and bactericidal activity. Furthermore, reduced levels of interferon-γ, which is necessary for enhancing macrophage antibacterial capabilities, result from defective natural killer cell activation. The activation of adaptive immune responses is delayed when this is coupled with impaired dendritic cell activity. Diabetes patients' antigen-presenting cells have increased intracellular oxidation, which modifies cytokine production and upsets the equilibrium of T-cell immunity. In diabetic hosts, the development of acute intracellular bacterial infections is associated with compromised T-cell-mediated immunity. Furthermore, people with diabetes frequently experience late hyper-inflammatory cytokine responses due to the increased intracellular bacterial load and the cumulative impact of chronic inflammation, which exacerbates systemic disease. Multidisciplinary study is necessary because the relationship between intracellular bacterial infections and diabetes poses new difficulties for immunologists.(31). Syndemic health issues like diabetes, insulin resistance (IR), and glucose intolerance are making this worldwide problem worse and increasing to a pandemic level. Ironically, even when hyperinsulinemia is present, illnesses with inflammatory components might result from decreased tissue sensitivity to insulin or IR.(32).

VI. ROLE OF INSULIN IN IMMUNITY SYSTEM

Almost all cellular functions depend on the availability of glucose, which is controlled by the vital hormone insulin(33). Immune cells also rely on insulin for their metabolic requirements and function, even though the cellular response to insulin has been thoroughly researched in the liver, skeletal muscle, and fat cells because of its involvement in controlling the availability of nutrients throughout the body. Particularly, effector and activated immune cells have higher energy requirements.(34). Therefore, immunity can be greatly impacted by any aberration in the body's insulin levels. The onset and advancement of metabolic disorders such diabetes, hypertension, cancer, and non-alcoholic fatty liver disease are all significantly influenced by insulin resistance. Genetics, weight, age, illnesses, and medication side effects all have an impact on the aetiology of insulin resistance. Mechanistically, insulin resistance can result from any factor that interferes with the insulin signalling pathway, such as anomalies in insulin receptors, changes in the internal environment (such as inflammation, hypoxia, lipotoxicity, and immunological responses), and deficiencies in the liver's and organelles' metabolic processes. Exercise, dietary changes, and chemotherapy using drugs such biguanides and glucagon-like peptide-1 serve as the cornerstones of contemporary therapy. approaches for insulin resistance. Acupuncture and herbal cures are examples of traditional Chinese medicine treatments that have demonstrated potential advantages. Even while our understanding of the mechanisms underlying insulin resistance has advanced, there are still unanswered questions. It is essential to find more accurate biomarkers for different chronic illnesses and lifestyle changes, as well as investigate natural or artificial medications that target insulin resistance. This strategy might result in more thorough treatment of metabolic disorders, which could lower medical expenses and enhance patients' quality of life. (35). (33). Obesity-related insulin resistance (IR) and glucose intolerance are typified by chronic inflammation, which is defined by T cell and macrophage infiltration into visceral adipose tissue (AT). Because hypertrophic adipocytes in obesity produce proinflammatory cytokines like IL-6 and TNF-α, which increase vascular permeability and attract cytotoxic T cells, including T cell phenotypes linked to IR, the cell-mediated immune response is especially noticeable in obese individuals . In fact, compared to obese individuals with IR (metabolically unhealthy obesity), insulin-sensitive (IS) patients with MHO show notable immunological changes in T cell morphologies. For instance, in older participants, the frequencies of naïve (CD45RA+ CCR7+ CD27+ CD28+) CD4+ and CD8+ T cell subsets were inversely correlated with HOMA-IR (homeostasis model assessment of insulin resistance) and positively correlated with ISI As established by the oral glucose tolerance test, the insulin sensitivity indextest (OGTT). Conversely, there was a negative correlation between ISI and the fraction of central memory (CD45RA− CD27+ CD28+) CD4+ T cells, and a positive correlation between ISI and HOMA-IR. Furthermore, there was a positive connection between HOMA-IR and the fraction of effector memory (CD45RA− CD27− CD28−) CD8+ T cells [230]. According to these results, the proportion of naïve CD4+ and CD8+ T cells may be a predictor of decreased insulin sensitivity. These findings lend credence to the idea that insulin-sensitive and insulin-resistant obese people can be distinguished by systemic inflammation metrics associated with T cell subtypes. Insulin-sensitive and insulin-resistant obese people are more likely to develop cardiometabolic disorders and should receive priority therapy for obesity.(36)(37)(38). Figure 1 summarizes the underlying causes of glucose intolerance.

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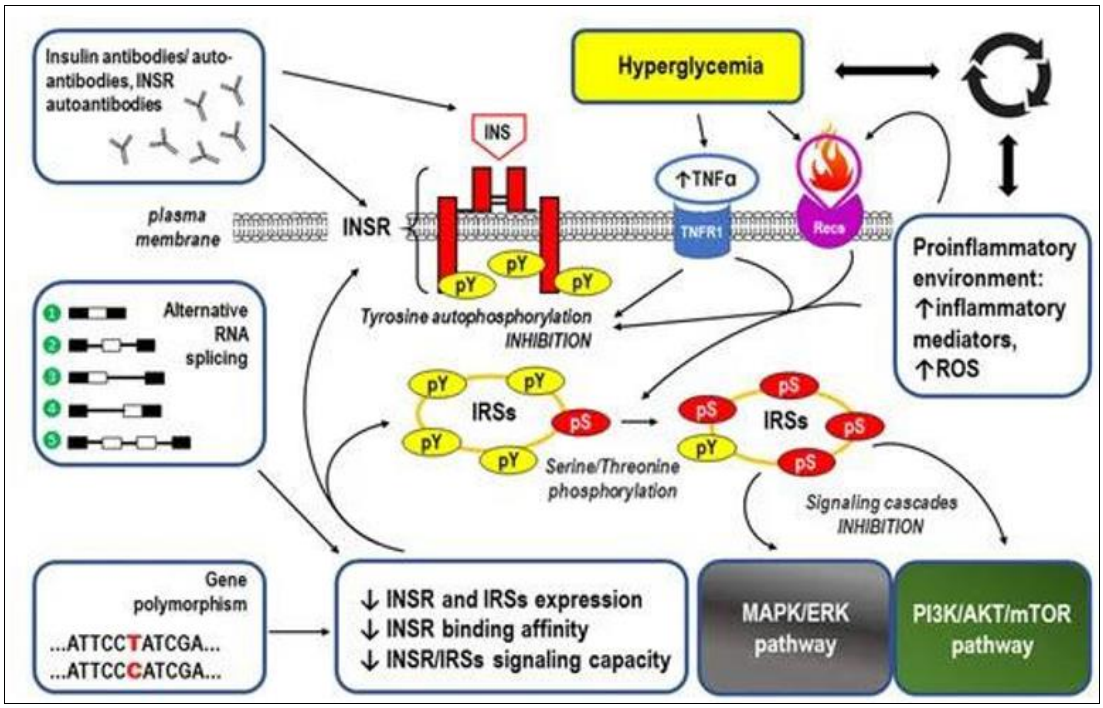

Fig 1. The Main Underlying Causes/Mechanisms of Insulin Resistance (IR)

VII. THE PATHOGENICITY OF *ACINETOBACTER BAUMANNII* IN POLYCYSTIC OVARIAN SYNDROME PATIENTS

In critical care settings around the world, infections with antibiotic-resistant *Acinetobacter* spp. are becoming more common. An insulin-cleaving protease is known to be produced by these bacteria. According to a study looking at how *Acinetobacter* spp. infections affect glucose metabolism, burn patients' development of glucose intolerance is significantly correlated with these infections. From January 2002 to March 2003, all 473 patients who were hospitalised to the Burns Centre had their data prospectively gathered. 3.4% of hospitalised patients experienced glucose intolerance during this time. Compared to those without the illness, individuals with an *Acinetobacter* spp. infection had a 9.8-fold increased risk of developing glucose intolerance. ($P < .0001$). This association remained significant even after adjusting for total body surface area (TBSA) burned ($P < .001$). Notably, 47% In contrast to 12% of patients with superficial infections, 12% of patients with deep Acinetobacter spp. infections had glucose intolerance ($P = .03$).

Furthermore, 27% of patients with pre-existing diabetes mellitus got *Acinetobacter* spp. infections, whereas only 8.5% of patients without diabetes had this ($P = .04$). *Acinetobacter* spp. infections and glucose intolerance in burn patients are clearly linked, according to this study(39).

A condition known as insulin resistance (IR) occurs when target organs do not react to insulin as well as they should. All phenotypes of polycystic ovarian syndrome (PCOS) share this common metabolic abnormality. Numerous epigenetic changes, such as DNA methylation, histone modifications, and miRNA expression, are believed to be the cause of IRinPCOSpatients.

Furthermore, environmental elements, Inflammation and dietary modifications are also factors in this process. Inflammation and dietary modifications are also factors in this process. Patients with polycystic ovarian syndrome (PCOS) may also have impaired insulin sensitivity as a result of vitamin D insufficiency. The hypothalamus's gonadotropin-releasing hormone (GnRH) gene is stimulated by compensatory hyperinsulinemia, which is brought on by insulin resistance (IR). The ovaries generate more androgen as a result of the pituitary gland producing luteinizing hormone pulses more frequently. Furthermore, by preventing the liver from synthesizing sex hormone-binding globulin (SHBG), hyperinsulinemia directly encourages the ovaries to make more androgens. Insulin resistance in a vicious loop, hyperinsulinemia, and hyperandrogenism in PCOS can result from this rise in androgen levels, which can also worsen insulin resistance.(40)(41)(42) .

According to a study, Gram-negative bacteria are more likely than Gram-positive isolates to cause urinary tract infections in women with PCOS. The most common bacterial isolates were *Escherichia coli* and *Acinetobacter baumannii*. The most resistant bacteria to both erythromycin and amoxicillin were *E. coli*. Patients with PCOS are more vulnerable to microbial infections because of elevated inflammation brought on by insulin resistance and other factors. Comparing these patients to those who are healthy, they frequently have a poorer intestinal mucosal barrier, less variety, and a different gut microbiota makeup, including lower levels of lactobacilli and bifidobacteria. Due to disturbed gut homeostasis, changes in gut microbiota have been associated with elevated inflammation and insulin

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resistance (43). Additionally, PCOS may result in modifications to the reproductive tract's microbial flora (44).

VIII. CONCLUSION

We conclude from this study that Acinetobacter baumannii, a common Gram-negative pathogenic bacterium, can cause serious illness and is resistant to a variety of drugs. We should also be aware that women of reproductive age are more likely to develop polycystic ovary syndrome (PCOS), which can present with a variety of symptoms. Insulin resistance is a result of hormonal and metabolic problems in women and can develop into type 2 diabetes. Because people with diabetes or insulin resistance are known to have weakened immune systems, the body becomes an ideal environment for a variety of microorganisms, including Acinetobacter baumannii.

REFERENCES

[1]. Kareem SM, Al-Alak SK, Khazaal SS, Najim SY, Aziz SN. Genetic detection of acinetobacter multidrug resistant isolates toward aminoglycoside and study the resistant to rifampicin/aminoglycoside combination. J Pharm Sci Res. 2018;10(6):1319–22.

[2]. Shi J, Cheng J, Liu S, Zhu Y, Zhu M. Acinetobacter baumannii: an evolving and cunning opponent. Front Microbiol. 2024;15:1332108.

[3]. Al-Kadmy IMS, Ali ANM, Salman IMA, Khazaal SS. Molecular characterization of Acinetobacter baumannii isolated from Iraqi hospital environment. New microbes new Infect. 2018;21:51–7.

[4]. Marino A, Augello E, Stracquadanio S, Bellanca CM, Cosentino F, Spampinato S, et al. Unveiling the Secrets of Acinetobacter baumannii: Resistance, Current Treatments, and Future Innovations. Int J Mol Sci. 2024;25(13):6814.

[5]. Shaheed HS, Jasim SY, Abbass WA-K. Studying some novel biochemical and immunological markers in a sample of Iraqi women with polycystic ovarian syndrome. Res J Pharm Technol. 2020;13(7):3171–8.

[6]. Deswal R, Narwal V, Dang A, Pundir CS. The prevalence of polycystic ovary syndrome: a brief systematic review. J Hum Reprod Sci. 2020;13(4):261–71.

[7]. Yang R, Li Q, Zhou Z, Qian W, Zhang J, Wu Z, et al. Changes in the prevalence of polycystic ovary syndrome in China over the past decade. Lancet Reg Heal Pacific. 2022;25.

[8]. Khalilov R, Abdullayeva S. MECHANISMS OF INSULIN ACTION AND INSULIN RESISTANCE. Adv Biol Earth Sci. 2023;8(2).

[9]. Perreault L, Newsom SA, Strauss A, Kerege A, Kahn DE, Harrison KA, et al. Intracellular localization of diacylglycerols and sphingolipids influences insulin sensitivity and mitochondrial function in human skeletal muscle. JCI insight. 2018;3(3).

[10]. Singh S, Pal N, Shubham S, Sarma DK, Verma V, Marotta F, et al. Polycystic ovary syndrome: etiology, current management, and future therapeutics. J Clin Med. 2023;12(4):1454.

[11]. Dunaif A, Segal KR, Futterweit W, Dobrjansky A. Profound peripheral insulin resistance, independent of obesity, in polycystic ovary syndrome. Diabetes. 1989;38(9):1165–74.

[12]. Nizar L, AL-Rekabi ANG. Hormonal Study of the different phenotypes of polycystic ovary syndrome. J Coll Basic Educ. 2016;22(93):101–8.

[13]. Barber TM, Wass JAH, McCarthy MI, Franks S. Metabolic characteristics of women with polycystic ovaries and oligo-amenorrhoea but normal androgen levels: implications for the management of polycystic ovary syndrome. Clin Endocrinol (Oxf). 2007;66(4):513–7.

[14]. Harrison CL, Lombard CB, Moran LJ, Teede HJ. Exercise therapy in polycystic ovary syndrome: a systematic review. Hum Reprod Update. 2011;17(2):171–83.

[15]. Li M, Chi X, Wang Y, Setrerrahmane S, Xie W, Xu H. Trends in insulin resistance: insights into mechanisms and therapeutic strategy. Signal Transduct Target Ther. 2022;7(1):216.

[16]. Wu H, Ballantyne CM. Metabolic inflammation and insulin resistance in obesity. Circ Res. 2020;126(11):1549–64.

[17]. Van der Kolk BW, Kalafati M, Adriaens M, Van Greevenbroek MMJ, Vogelzangs N, Saris WHM, et al. Subcutaneous adipose tissue and systemic inflammation are associated with peripheral but not hepatic insulin resistance in humans. Diabetes. 2019;68(12):2247–58.

[18]. Trouwborst I, Wouters K, Jocken JW, Jardon KM, Gijbels A, Dagnelie PC, et al. Circulating and adipose tissue immune cells in tissue-specific insulin resistance in humans with overweight and obesity. Obesity. 2023;31(5):1326–37.

[19]. Sethi JK, Hotamisligil GS. Metabolic messengers: tumour necrosis factor. Nat Metab. 2021;3(10):1302–12.

[20]. Chapman NM, Chi H. Metabolic adaptation of lymphocytes in immunity and disease. Immunity. 2022;55(1):14–30.

[21]. Friedrich K, Sommer M, Strobel S, Thrum S, Blüher M, Wagner U, et al. Perturbation of the monocyte compartment in human obesity. Front Immunol. 2019;10:1874.

[22]. Krinninger P, Ensenauer R, Ehlers K, Rauh K, Stoll J, Krauss-Etschmann S, et al. Peripheral monocytes of obese women display increased chemokine receptor expression and migration capacity. J Clin Endocrinol Metab. 2014;99(7):2500–9.

[23]. Devêvre EF, Renovato-Martins M, Clément K, Sautes-Fridman C, Cremer I, Poitou C. Profiling of the three circulating monocyte subpopulations in human obesity. J Immunol. 2015;194(8):3917–23.

[24]. Crommen S, Simon M-C. Microbial regulation of glucose metabolism and insulin resistance. Genes (Basel). 2017;9(1):10.

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/25may343

[25]. Perera D, Kleinstein SE, Hanson B, Hasturk H, Eveloff R, Freire M, et al. Impaired host response and the presence of Acinetobacter baumannii in the serum microbiome of type-II diabetic patients. Iscience. 2021;24(1).
[26]. Darwitz BP, Genito CJ, Thurlow LR. Triple threat: how diabetes results in worsened bacterial infections. Infect Immun. 2024;e00509-23.
[27]. Leung C-H, Liu C-P. Diabetic status and the relationship of blood glucose to mortality in adults with carbapenem-resistant Acinetobacter baumannii complex bacteremia. J Microbiol Immunol Infect. 2019;52(4):654–62.
[28]. Bharadwaj A, Rastogi A, Pandey S, Gupta S, Sohal JS. Multidrug-Resistant Bacteria: Their Mechanism of Action and Prophylaxis. BioMed Research International, 2022, 17. 2022;
[29]. Matta-Gutierrez G, Garcia-Morales E, Garcia-Alvarez Y, Álvaro-Afonso FJ, Molines-Barroso RJ, Lazaro-Martinez JL. The influence of multidrug-resistant bacteria on clinical outcomes of diabetic foot ulcers: a systematic review. J Clin Med. 2021;10(9):1948.
[30]. Adeyemo AT, Kolawole B, Rotimi VO, Aboderin AO. Multicentre study of the burden of multidrug-resistant bacteria in the aetiology of infected diabetic foot ulcers. Afr J Lab Med. 2021;10(1):1–10.
[31]. Hodgson K, Morris J, Bridson T, Govan B, Rush C, Ketheesan N. Immunological mechanisms contributing to the double burden of diabetes and intracellular bacterial infections. Immunology. 2015;144(2):171–85.
[32]. Szukiewicz D. Molecular mechanisms for the vicious cycle between insulin resistance and the inflammatory response in obesity. Int J Mol Sci. 2023;24(12):9818.
[33]. Boucher J, Kleinridders A, Kahn CR. Insulin receptor signaling in normal and insulin-resistant states. Cold Spring Harb Perspect Biol. 2014;6(1):a009191.
[34]. Van Niekerk G, Christowitz C, Conradie D, Engelbrecht A-M. Insulin as an immunomodulatory hormone. Cytokine Growth Factor Rev. 2020;52:34–44.
[35]. Zhao X, An X, Yang C, Sun W, Ji H, Lian F. The crucial role and mechanism of insulin resistance in metabolic disease. Front Endocrinol (Lausanne). 2023;14:1149239.
[36]. Exley MA, Hand L, O'Shea D, Lynch L. Interplay between the immune system and adipose tissue in obesity. J Endocrinol. 2014;223(2):R41–8.
[37]. Villarreal-Calderón JR, Cuéllar RX, Ramos-González MR, Rubio-Infante N, Castillo EC, Elizondo-Montemayor L, et al. Interplay between the adaptive immune system and insulin resistance in weight loss induced by bariatric surgery. Oxid Med Cell Longev. 2019;2019(1):3940739.
[38]. Bensussen A, Torres-Magallanes JA, Roces de Álvarez-Buylla E. Molecular tracking of insulin resistance and inflammation development on visceral adipose tissue. Front Immunol. 2023;14:1014778.
[39]. Furniss D, Gore S, Azadian B, Myers SR. Acinetobacter infection is associated with acquired glucose intolerance in burn patients. J Burn Care Rehabil. 2005;26(5):405–8.
[40]. Zhao H, Zhang J, Cheng X, Nie X, He B. Insulin resistance in polycystic ovary syndrome across various tissues: an updated review of pathogenesis, evaluation, and treatment. J Ovarian Res. 2023;16(1):9.
[41]. Dumesic DA, Oberfield SE, Stener-Victorin E, Marshall JC, Laven JS, Legro RS. Scientific statement on the diagnostic criteria, epidemiology, pathophysiology, and molecular genetics of polycystic ovary syndrome. Endocr Rev. 2015;36(5):487–525.
[42]. Azziz R, Carmina E, Chen Z, Dunaif A, Laven JSE, Legro RS, et al. Polycystic ovary syndrome. Nat Rev Dis Prim. 2016;2(1):1–18.
[43]. Hong X, Qin P, Huang K, Ding X, Ma J, Xuan Y, et al. Association between polycystic ovary syndrome and the vaginal microbiome: a case-control study. Clin Endocrinol (Oxf). 2020;93(1):52–60.
[44]. Marquardt RM, Kim TH, Shin J-H, Jeong J-W. Progesterone and estrogen signaling in the endometrium: what goes wrong in endometriosis? Int J Mol Sci. 2019;20(15):3822.