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RESEARCH ARTICLE

PSORIASIS AND PREGNANCY CHALLENGES AND RISKS

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Abstract

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Introduction:-

Psoriasis multifactorial complex chronic inflammatory skin disease characterized by infiltration of inflammatory cells into the epidermis and altered keratinocyte differentiation(1), causes erythematous, scaly patches, and plaques that can affect any part of the body(2), affects both sexes equally , although women generally develop the disease earlier than men(3),Psoriasis onset occur at any age, with the mean age of presentation in females at 26.94 ± 14.94 years(4,5,6,7,).

Various environmental risk factors, including trauma to the skin, infections, obesity, smoking, alcohol use, emotional stress, and various drugs, have been associated with psoriasis(8,9).

psychosocial issues related to psoriasis reveal several important insights that clinicians should bear in mind when treating adult women(10).

Course of Psoriasis During Pregnancy :

Most pregnant women had improvement in psoriasis due to immunomodulatory changes from increased oestrogen, whereas some women's psoriasis worsens with pregnancy(11).

The maternal immune system undergoes physiological changes to achieve tolerance to antigens expressed by fetal cells and prevent rejection of the fetus. These changes influenced by the effect of estrogens, progesterone, and cortisol, and gradually increase blood levels during pregnancy, giving rise to a change in helper T (TH) cell polarization that potentiates the humoral TH 2 response and inhibits the cell-mediated TH 1 response(12).

The close relationship between the embryo and the endometrium and the placenta and the decidua mediated by steroid hormones ,and diverse cytokines and chemokines, to ensure successful maintenance of pregnancy(13,14).

The cytokines levels progressively decrease during the second and third trimesters of pregnancy as the placenta completes its formation. In the last weeks of pregnancy, the balance of cytokines is once again reversed towards a

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predominance of TH1 cells, which stimulate labor and protect both the mother and fetus from infection during and after birth.(15).

In between 30% and 40% of women with psoriasis experience clinical improvements during pregnancy and between 40% and 90% worsening of disease between week 4 and 6 postpartum(16).

Increased levels of diverse proinflammatory cytokines (IL-6 and TNF) and inflammation biomarkers (C-reactive protein) in both maternal serum and cord blood during the pregnancy of women with psoriasis have been shown to result in preterm birth or small-for-gestational-age neonates.(17).

During pregnancy, the maternal immune system shifts from a T helper cell Th1 to a Th2 response. With this shift, certain Th2-mediated diseases such as lupus erythematosus worsen during pregnancy(18,19,20,21).

The Th2 immune response that potentiated by estrogen, increase the concentrations of interleukin IL-4, IL- 5, and IL-10, while androgens have been found to increase the Th1 response leading to increased IL-2 production and activation of CD8+ T-cells, these differences marked in reproductive years but disappear after menopause(22,23).

Interactions of estrogen and prolactin (PRL), have an important role in modulating the immune response(24,25),It interferes with B-cell tolerance induction, enhances proliferative response to antigens and mitogens, and increases the production of immune globulins, cytokines, and autoantibodies. Patients with hyperprolactinemia (HPRL) present with many different clinical manifestations, one of them is psoriasis.(26,27).

It has been observed that worsening of symptoms occurs when estrogen and progesterone levels drop postpartum,prior to menses, and at menopause, while most patients receiving hormone therapy around menopause noted no change in their condition(28,29,30).

pregnancy and hormonal changes lead to improvement of psoriasis; because the estrogens have both an immunosuppressive and immunostimulatory property promoting a state of immune tolerance(31).

The progesterone levels alone did not correlate with change in psoriasis and therefore it can be assumed that patients who experience an improvement of psoriasis have higher levels of estrogen relative to progesterone during pregnancy, whereas those who have lower ratio levels will remain unchanged or potentially worsen(32). patients with psoriasis presented with a flare-up of symptoms within six weeks of delivery, which correlates with the previously mentioned observations implicating the role of hormones in psoriatic symptoms(33,34).

Management of Psoriasis During Pregnancy

U.S. Food and Drug Administration (FDA) pregnancy categories:

1. A, large studies suggest no evidence of harm.
2. B, animal adverse effects and human studies fail to show adverse effects.
3. C, animal studies show adverse risks, but no adequate human studies.
4. D, evidence of human fetal risk from human studies or marketing or investigational experiences.
5. X, evidence that the drug causes harm to the fetus, the risks clearly outweigh the benefits for pregnant women(35).

Interruption of any therapy is reasonable strategy for psoriasis that improves during pregnancy, in consideration that common forms of psoriasis are not compromise the maternal and fetal health.

The discontinuation can be impractical with severe psoriasis, but the teratogenic and other possible risks should be balanced with the risk of uncontrolled inflammation that affecting the course of pregnancy and postpartum period. A woman with psoriasis of reproductive age should be asked about her childbearing planning to get an appropriate medications and healthy education(36).

Topical treatments:

Moisturizers and emollients, such as petroleum jelly, should be tried first, because these are known to be safe(37).

Topical Corticosteroids(FDA Category C):

The most commonly used therapy for localized psoriatic plaques generally and also in pregnancy, and associated with little, if any, teratogenic risk, in conservative warn pregnant women not to use large amounts of topical corticosteroids over extensive parts of the body because of the possibility of having a new- born with low birth weight(38).

Low- to moderate-potency topical corticosteroids are next step, followed by high-potency topical corticosteroids, only if necessary, in the second and third trimesters, and risks of high-potency topical steroids applied on large body surface areas increased potential for systemic absorption(39).

Salicylic acid (No FDA Pregnancy Category):

After topical application of salicylic acid or its derivatives, between 9% and 25% of salicylic acid has been reported to be systemically absorbed(40), and its use was linked to premature ductus arteriosus constriction(41).

Topical retinoids (tazarotene) (FDA Category X):

Approved for the treatment of psoriasis but it is recommended that tazarotene should be stopped immediately if the woman becomes pregnant while using it(42).

Calcipotriene (FDA Category C):

Approximately 6% of calcipotriene, (a synthetic vitamin D3 derivative), is absorbed systemically when the ointment is applied onto psoriatic plaques(43),Studies in animals have shown an increased incidence of skeletal abnormalities and incomplete ossification of pelvic bones and phalanges of affected fetuses(44).

Tacrolimus(FDA Category C):

Systemic absorption of tacrolimus after topical application is very low and is not associated with systemic effects . There are no literature reports on women using tacrolimus topically during pregnancy(45).

UVB phototherapy (No FDA Pregnancy Category):

considered to be a safe and effective form of treatment for psoriasis in pregnancy and there are no contraindications for its use(46).

Coal tar (No FDA Pregnancy Category):

Despite the potential risks that have emerged from animal studies with coal tar, the literature on human exposure has failed to reveal any developmental effects.The results of a retrospective study suggested that coal tar should be prohibited during the first trimester of pregnancy and, at the most, limited during the second and third trimesters (47).

Systemic treatments:

If moderate-to-severe psoriasis remains active or worsens during pregnancy, there might be a need for systemic treatment, and making the appropriate treatment decision can be difficult.

Systemic corticosteroids (FDA category C):

not routinely used in common forms of psoriasis, but they can be used in selected cases or in patients with concomitant arthritis, and are considered a treatment of choice for impetigo herpetiformis.(48).

PUVA (FDA category C):

(photochemotherapy) is contraindicated in pregnancy because both components in PUVA treatment, the oral medication psoralen and the UVA light, are potentially mutagenic(49).

Despite the theoretical mutagenic and teratogenic effect of treatment evidence seems to indicate that it apparently does not carry any significant risk for abnormal delivery outcome(50,51).

Systemic retinoids (Acitretin) (FDA category X):

The relative risk of fetal malformation in pregnancies exposed to an oral retinoid in early pregnancy is 25.6 times that in the general population(52).

Methotrexate (FDA Category X):

is absolutely contraindicated in pregnancy, as it is known to be an abortifacient, mutagenic and teratogenic agent. The sensitive period for the occurrence of malformations is between 6 and 8 weeks after conception and the dose required to produce defects is greater than 10 mg per week and some time less than 10 mg(53).

Men as well as women should be counseled to use effective contraception while being treated with methotrexate. It is recommended to interrupt the drug for at least 3 months before conception for both men and women.(54).

Cyclosporine (FDA category C):

There are limited data on the effect of ciclosporin in pregnant psoriasis patients, and the majority of information on its use during pregnancy derives from registries of transplant recipients, who usually receive higher doses than psoriasis patients, The drug has no mutagenic properties, no increase of congenital malformations nor any special malformation pattern has been noted. However, there was an increased risk of premature delivery and low birth weight(55,56), the current recommendation is that breastfeeding should be avoided while taking ciclosporin due to concerns of immunosuppression in the infant(57).

Biologic therapy (FDA category B):

Exposure of the fetus to biologic agents during pregnancy depends on the transport across the placenta. Immunoglobulin G (IgG) is the only major class of antibody that is transported across the human placenta. In the first two trimesters of pregnancy fetal levels of IgG in umbilical venous blood are low and not surpass maternal levels of IgG until the beginning of the third trimester when active transport of the IgG molecules across the placenta increases rapidly(58), treatment of patients with anti-tumor necrosis factor (TNF) alpha biologic medications is generally considered safe during the first half of pregnancy(59).

Patients with psoriasis who continue treatment with biologic agents during their pregnancy and particularly into the third trimester should be informed of impaired immune response in their newborn infants(60).

A large collection of 131 pregnancies exposed to infliximab from the Centocor safety database reported no increased risk of adverse outcomes such as miscarriages, therapeutic terminations of pregnancy, and congenital malformations when compared with the general population(61).

The OTIS (Organization for Teratology Information Specialists) registry reported 100 pregnancies exposed to etanercept, which had similar live birth rates and similar rates of major congenital malformations to control group of pregnant patients with inflammatory arthritis not exposed to etanercept (62).

The same registry reported 66 pregnancies exposed to adalimumab for rheumatoid arthritis during the first trimester, comparing them to non-adalimumab treated patients and healthy controls. There was no increased risk or evidence of a specific pattern of major or minor birth defects connected with adalimumab exposure(63).

Ustekinumab is a relatively new biologic drug and experience during pregnancy is extremely limited(64).

Breastfeeding during therapy with biologics is not generally recommended, although the levels of the drugs detectable in breast milk are significantly lower than those in maternal circulation.

Most package inserts for medications warn against breastfeeding while being treated with biologic agents, but recent data shows that breastfeeding may overall be safe for nursing mothers without significant risk to newborn babies. Low levels of TNF-alpha inhibitors can be detected in breast milk(65).

However, biologics may be used only in high-need situations and when no alternative treatments are available(66).

Conclusion:-

In managing psoriasis across the life span, several fundamental principles must be considered. First, both clinicians and patients should remember that although psoriasis is a chronic, lifelong disease, effective treatment is available. Further, a wide range of therapeutic options is available, allowing for optimal, individualized therapy. In addition to choosing the most effective therapeutic agents, clinicians must help patients manage all aspects of the disease, including the psychosocial impact/manifestations of psoriasis. This includes educating them and their families, identifying social problems and potential compliance issues, and being aware of school and work challenges that patients with psoriasis may face. Clinicians should recommend counseling and/or patient support groups, when

indicated, providing patients and their families with information about the resources available. Finally, it is crucial to discuss family planning with patients who are of childbearing age.

Reference:-

1. Liu Y, Krueger JG, Bowcock AM. Psoriasis: genetic associations and immune system changes. *Genes and Immunity* 2007;8:1-12.
2. M. A. Johnson and A. W. Armstrong, "Clinical and histologic diagnostic guidelines for psoriasis: a critical review," *Clinical Reviews in Allergy Immunology*, vol. 44, 2, pp. 166–172, 2013.
3. Levine D, Gottlieb A. Evaluation and management of psoriasis: An internist's guide. *Med Clin North Am*. 2009;93: 1291-303.
4. Busch AL, Landau JM, Moody MN. Pediatric psoriasis. *Skin Ther Lett*. 2012;17:5-7).
5. M. T. Islam, H. K. Paul, S. M. Zakaria, M. M. Islam, and M. Shafiquzzaman, "Epidemiological determinants of psoriasis," *Mymensingh Medical Journal*, vol. 20, no. 1, pp. 9–15, 2011.)
6. Parisi R, Symmons DP, Griffiths CE, Ashcroft DM. Global epidemiology of psoriasis: a systematic review of incidence and prevalence. *J Invest Dermatol* 2013; 133:377–85.).
7. Tauscher AE, Fleischer AB, Phelps KC, Feldman SR. Psoriasis and pregnancy. *J Cutan Med Surg* 2002;6:561–70.).
8. Tauscher AE, Fleischer AB Jr, Phelps KC, Feldman SR. Psoriasis and pregnancy. *J Acta Dermatovenerol Croat* 2009;17(3):193-197 *Cutan Med Surg* 2002;6:561-70.).
9. M. Gupta and A. Gupta, "Psychological factors and psoriasis," in *Epidemiology, Causes and Prevention of Skin Diseases*, J. J. Grob, R. Stern, R. Mackie, and W. Weinstock, Eds., pp. 129–141, Blackwell Science, Oxford, UK, 1997.)
10. National Psoriasis Foundation. Spring 2005: Survey panelsnapshot.<http://www.psoriasis.org/document.doc?id=377>. Accessed February 4, 2014.).
11. Weatherhead S, Robson SC, Reynolds NJ. Management of psoriasis in pregnancy. *BMJ* 2007; 334:1218–20.).
12. Doria A, Iaccarino L, Arienti S, Ghirardello A, Zampieri S, Rampudda ME, et al. Th2 immune deviation induced by pregnancy: The two faces of autoimmune rheumatic diseases. *Reprod Toxicol*. 2006;22:234-41.).
13. Murase J, Chan KK, Garite TJ, Cooper DM, Weinstein GD. Hormonal effect on psoriasis in pregnancy and post partum. *Arch Dermatol*. 2005;141:601-6.
14. Shigeru S. Cytokine cross-talk between mother and the embryo/placenta. *J Reprod Immunol*. 2001;52: 15-33.).
15. Bandoli G, Johnson DL, Jones KL, Lopez Jimenez J, Salas E, Mirrasoul N, et al. Potentially modifiable risk factors for adverse pregnancy outcomes in women with psoriasis. *Br J Dermatol*. 2010;163:334-9.)
16. Raychaudhuri SP, Navare T, Gross J, Raychaudhuri SK. Clinical course of psoriasis during pregnancy. *Int J Dermatol*. 2003;42:518-20.).
17. Lima X, Janakiraman V, Hughes M, Kimball A. The impact of psoriasis on pregnancy outcomes. *J Invest Dermatol*. 2012;132:85-91.).
18. Ruiz V, Manubens E, Puig L. Psoriasis in pregnancy: A review (I). *Actas Dermosifiliogr* 2014;105:734–43.).
19. S. Coimbra, A. Figueiredo, E. Castro, P. Rocha-Pereira, and A. Santos-Silva, "The roles of cells and cytokines in the pathogenesis of psoriasis," *International Journal of Dermatology*, vol. 51, no. 4, pp. 389–398, 2012.).
20. A. Pietrzak, B. Leczewicz-Torun', and A. Jakimiuk, "Lipid and hormone profile in psoriatic females," *Annales Universitatis Mariae Curie-Skłodowska. Sectio D*, vol. 57, no. 2, pp. 478–483, 2002.).
21. N. Kanda and S. Watanabe, "Regulatory roles of sex hormones in cutaneous biology and immunology," *Journal of Dermatological Science*, vol. 38, no. 1, pp. 1–7, 2005.).
22. L. M. Pennell, C. L. Galligan, and E. N. Fish, "Sex affects immunity," *Journal of Autoimmunity*, vol. 38, no. 2-3, pp. J282–J291, 2012.).
23. J. L. Landau, M. N. Moody, N. Kazakevich, and L. H. Goldberg, "Psoriasis and the pregnant woman: what are the key considerations?" *Skin Therapy Letter*, vol. 16, no. 9, pp. 1–3, 2011.).
24. Engineer L, Bhol K, Ahmed AR. Pemphigoid gestationis: A review. *Am J Obstet Gynecol*. 2000;183:483-91.).
25. Barankin B, Silver SG, Carruthers A. The skin in pregnancy. *J Cutan Med Surg*. 2002;6:236-40.)
26. S. Shelly, M. Boaz, and H. Orbach, "Prolactin and autoimmunity," *Autoimmunity Reviews*, vol. 11, no. 6-7, pp. A465–A470, 2012.)
27. F. S. Dhabhar, "Psychological stress and immunoprotection versus immunopathology in the skin.," *Clinics in Dermatology*, vol. 31, no. 1, pp. 18–30, 2013).
28. C. M. Mowad, D. J. Margolis, A. C. Halpern, B. Suri, M. Synnestvedt, and C. A. Guzzo, "Hormonal influences on women with psoriasis," *Cutis*, vol. 61, no. 5, pp. 257–260, 1999.

29. A. S. Boyd, L. F. Morris, C. M. Phillips, and M. A. Menter, "Psoriasis and pregnancy: hormone and immune system interaction," *International Journal of Dermatology*, vol. 35, no. 3, pp. 169–172, 1996.
30. [R. Ceovic, J. Lipozencic, A. Pasic, and K. Kostovic, "Psoriasis in pregnancy: a review of most important literature data," *Acta DermatovenerologicaCroatica*, vol. 17, no. 3, pp. 193–197, 2009.)]
31. H. Carlsten, N. Nilsson, R. Jonsson, K. Backman, R. Holmdahl, and A. Tarkowski, "Estrogen accelerates immune complex glomerulonephritis but ameliorates T cell-mediated vasculitis and sialadenitis in autoimmune MRL lpr/lpr mice," *Cellular Immunology*, vol. 144, no. 1, pp. 190–202, 1992.)
32. J. E. Murase, K. K. Chan, T. J. Garite, D. M. Cooper, and G. D. Weinstein, "Hormonal effect on psoriasis in pregnancy and post partum," *Archives of Dermatology*, vol. 141, no. 5, pp. 601–606, 2005).
33. S. Weatherhead, S. C. Robson, and N. J. Reynolds, "Management of psoriasis in pregnancy," *British Medical Journal*, vol. 334, no. 7605, pp. 1218–1220, 2007.)
34. S. Kar, A. Krishnan, and P. V. Shivkumar, "Pregnancy and skin," *The Journal of Obstetrics and Gynecology of India*, vol. 62, no. 3, pp. 268–275, 2012.)
35. Murase JE, Heller MH, Butler DC. Safety of dermatologic medications in pregnancy and lactation: part I. Pregnancy. *J Am Acad Dermatol* 2014; 70:401.e1–14.)
36. Y. S. C. Bae, A. S. Van Voorhees, S. Hsu et al., "Review of treatment options for psoriasis in pregnant or lactating women: from the medical board of the national psoriasis foundation," *Journal of the American Academy of Dermatology*, vol. 67, no. 3, pp. 459–477, 2012.
37. Weatherhead S, Robson SC, Reynolds N. Management of psoriasis in pregnancy. *BMJ* 2007;334:1218-20.)
38. Lam J, Polifka JE, Dohil AM. Safety of dermatologic drugs used in pregnant patients with psoriasis and other inflammatory skin diseases. *J Am Acad Dermatol* 2008;59:295- 315.
39. Tyler KH, Zirwas MJ. Pregnancy and dermatologic therapy. *J Am Acad Dermatol*. 2013;68(4):663–671. [PubMed].
40. Murase JE, Heller MM, Butler DC. Safety of dermatologic medications in pregnancy and lactation: Part I. Pregnancy. *J Am Acad Dermatol*. 1.2014;70(3):401.e1-e14. [PubMed].
41. Morra P, Bartle WR, Walker SE, Lee SN, Bowles SK, Reeves RA. Serum concentrations of salicylic acid following topically applied salicylate derivatives. *Ann Pharmacother* 1996;30:935-40.
42. Torloni MR, Cordioli E, Zamith MM, Hisaba WJ, Nardoza LM, Santana RM, et al. Reversible constriction of the fetal ductus arteriosus after maternal use of topical diclofenac and methyl salicylate. *Ultrasound ObstetGynecol*. 2006;27: 227-9.
43. Tauscher AE, Fleischer AB Jr, Phelps KC, Feldman SR. Psoriasis and pregnancy. *J Acta Dermatovenerol Croat* 2009;17(3):193-197
44. *Cutan Med Surg* 2002;6:561-70.
45. Koo YM. Current consensus and update on psoriasis therapy: a perspective from the United States. *J Dermatol* 1999;26:723-33.
46. Dovonex label (Bristol-Myers Squibb). [accessed 6 Jun 2013]. Available in: <http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=13916cd3-6fe6-401e-af71-07ae2686bce0>.
47. Soter NA, Fleischer AB, Webster GF. Tacrolimus ointment for the treatment of atopic dermatitis in adult patients: part II, Safety. *J Am Acad Dermatol* 2001;44:S39-S46.
48. Bridges BA. An estimate of genetic risk from 8-methoxypsoralen photochemotherapy. *Hum Genet* 1979;49:91-6.
49. Franssen ME, van der Wilt GJ, de Jong PC, Bos RP, Arnold WP. A retrospective study of the teratogenicity of dermatological coal tar products. *Acta DermVenereol*. 1999;79(5):390–391
50. Armenti VT, McGroary CH, Cater JR, Radomski JS, Moritz MJ. Pregnancy outcomes in female transplant recipients. *Transplant Proc*. 1998;30(5):1732–1734. [PubMed] [Google Scholar].
52. Spuls PI, Bossuyt PM, van Everdingen JJ. The development of practice guidelines for the treatment of severe plaque-form psoriasis. *Arch Dermatol* 1998;134:1591-6.
53. Stern RS, Lange R. Outcomes of pregnancies among women and partners of men with a history of exposure to methoxsalen- photochemotherapy (PUVA) for the treatment of psoriasis. *Arch Dermatol*. 1991;127(3):347–350.
54. Gunnarskog JG, Källén AJ, Lindelöf BG, Sigurgeirsson B. Psoralen photochemotherapy (PUVA) and pregnancy. *Arch Dermatol*.
55. Lammer EJ, Chen DT, Hoar RM, Agnish ND, Benke PJ, Braun JT. Retinoic acid embryopathy. *N Engl J Med* 1985;313:837-41.
56. Kozlowski RD, Steinbrunner JV, MacKenzie AH, Clough JD, Wilke WS, Segal AM. Outcome of first-trimester exposure to low-dose methotrexate in eight patients with rheumatic disease. *Am J Med*. 1990;88:589-92.

57. Lam J, Polifka JE, Dohil MA. Safety of dermatologic drugs used in pregnant patients with psoriasis and other inflammatory skin diseases. *J Am Acad Dermatol.* 2008;59(2):295–315.
58. Perales-Puchalt A, Vila Vives JM, Lopez Montes J, DiagoAlmela VJ, Perales AJ. Pregnancy outcomes after kidneytransplantation-immunosuppressive therapycomparison. *Matern Fetal Neonatal Med.* 2012;25:1363-6.
59. Bar Oz B, Hackman R, Einarson T, Koren G. Pregnancy outcome after cyclosporinotherapy during pregnancy: a meta-analysis. *Transplantation.* 2001;71:1051-5.
60. Moretti ME, Sgro M, Johnson DW, Sauve RS, Woolgar MJ, Taddio A, et al. Cyclosporine excretion into breast milk. *Transplantation.* 2003;75:2144-6.
61. Chambers CD, Johnson DL. Emerging data on the use of anti-tumor necrosis factor- alpha medications in pregnancy. *Birth Defects Res A Clin Mol Teratol* 2012;94: 607–11.
62. Förger F, Villiger PM. Treatment of rheumatoid arthritis during pregnancy: Present and future. *Expert Rev Clin Immunol* 2016;12:937–44.
63. Cheent K, Nolan J, Shariq S, Kiho L, Pal A, Arnold J. Case report: Fatal case of disseminated BCG infection in an infant born to a mother taking infliximab for Crohn's disease. *J Crohns Colitis* 2010;4:603–5.
64. Katz JA, Antoni C, Keenan GF, Smith DE, Jacobs SJ, Lichtenstein GR. Outcome ofpregnancy in women receiving infliximab for the treatment of Crohn's diseaseand rheumatoid arthritis. *Am J Gastroenterol.* 2004;99:2385-92.
65. Johnson DL, et al. Pregnancy outcomes in women exposed to etanercept: the OTIS Autoimme Diseases in Pregnancy Project. *Arthritis Rheum.* 2008;58:Abstract 1387.
66. Chambers CD, et al. Pregnancy outcomes in women exposed to adalimum- ab for the treatment of rheumatoid arthritis. *Pharmacoepidemiol Drug Saf.* 2012;21(Suppl 3):377.
67. Andrulonis R, Ferris LK. Treatment of severe psoriasis with ustekinumab during pregnancy. *J Drugs Dermatol* 2012;11:1240-1.
68. Ben-Horin S, Yavzori M, Katz L, Picard O, Fudim E, Chowers Y, et al. Adalimumab level in breast milk of a nursing mother. *ClinGastroenterol Hepatol.* 2010;8:475-matory bowel disease. *Clin Gastroenterol Hepatol.* 2013;11:286-92. 6.
69. Yiu, Z.Z.; Griffiths, C.E.; Warren, R.B. Safety of biological therapies for psoriasis: Effects on reproductive potential and outcomes in male and female patients. *Br. J. Dermatol.* 2014, 171, 485–491.