

AYURVEDA, EPIGENETICS AND FEMALE INFERTILITY

Dr. Aishwarya Bongane^{1*}, Dr. Jana Avhad² and Dr. Vidhya Sarode³Pg Scholar¹, Assistant Professor², Hod Stirog Evum Prasutitantra³,

Department of Stiroga Evum Prasuti Tantra A.R.A.H. Manchi Hills, Sangamner.

Article Received on
07 February 2023,Revised on 28 Feb. 2023,
Accepted on 20 March 2023

DOI: 10.20959/wjpr20235-27530

Corresponding Author*Dr. Aishwarya Bongane**Pg Scholar, Department of
Stiroga Evum Prasuti Tantra
A.R.A.H. Manchi Hills,
Sangamner.**1. ABSTRACT**

The concepts of survival and adaptability comes only when the modern era goes hand in hand with the ancient wisdom. This article deals with the correlation of new concept which gave a brand new path to the world of genetics i.e. epigenetics and our vedic knowledge i.e. ayurveda in view of female infertility. Epigenetics is the study of how person's behaviour and environment can cause changes that affect the way one's genes work.^[1] Unlike genetic changes, epigenetic changes are reversible and do not change the DNA sequence, but they can change how body reads a DNA sequence. This article primarily deals with the core 4 external factors that cause epigenetic changes and are mainly responsible for infertility i.e. 1) Diet 2) Stress 3) Night shift 4)

Environmental changes, While ayurveda has already described the idea of epigenetic changes in the form of *prakruti* in *Charak indriya sthana*^[2] and even mentioned the methods to prevent it and give birth to healthy progeny.

KEYWORDS: Epigenetics, *prakruti*, DNA, chromatin remodeling, histone modification, microRNA.

2. INTRODUCTION

Epigenetics is the study of changes in organisms caused by modification of gene expression rather than alternation of the genetic code itself.^[3] The term epigenetics sounds new to us, but our *Acharyas* have described the mechanism of epigenetics ages before that is far beyond our imagination.

तत्र प्रकृतिर्जातिप्रसक्ता च, कुलप्रसक्ता च, देशानुपातिनी च, कालानुपातिनी च, वयोऽनुपातिनी च, प्रत्यात्मनियता चेति । च. इं. १/५[2]

Acharya charak clearly mentioned that the external factors like *kala, desh, vaya, kul, jaati* affect the *prakruti* (genome) of an individual and this what exactly epigenetics mean. Various lifestyle modifications like following *Dinacharya, Ritucharya, Ratricharya* which are scattered throughout the *Samhitas* prove to be extremely useful in modern era related gynecological problems.

Firstly focusing on to the basic knowledge of human's basic genetic makeup, all nucleated cells are made up of DNA and the combination of DNA creates genes. It is estimated that humans have approximately 20, 000 genes. Less than 2% of these are coding genes that express themselves and are known as genotype.

Genotype refers to entire set of genes in the cells of an organism which makes the genetic constitution of the individual. The genotype is responsible for the phenotype of the individual. Phenotype is the set of observable characteristics of an individual.^[4]

In ayurveda genotype is related to the basic structural constitution i.e. the *Mahabhutas*-

गर्भस्तुखल्वतरिक्षवायुग्नि तोयभूमिविकारचेतनाधिष्ठानभूत | च. शा. ४/६^[5]

Even the genotype is based on the factors that are responsible for the formation of new life i.e. *Garbha*.

शुक्रशोणितजीवसंयोगे तु खलु कुक्षिगते गर्भसंज्ञा भवति | च. शा. ४/५^[6]

In the same way, phenotype is related to the external factors that an individual is exposed to or where the individual is born or in which community he is born.

The modern day research provides basics of correlation between genes and *prakruti* for example, phosphoglucomutase 1 (PGM1) gene has been correlated with *Pittaprakruti*.^[7] Even a reasonable correlation has been established between HLA and *prakruti* type.^[8] This article deals with 4 major factors 1)Diet 2)environmental changes 3)night shifts 4)stress that cause epigenetic changes in female reproductive system and are responsible for causing female infertility.

3. MATERIAL AND METHODS

MATERIAL-Only literary material i.e. ayurvedic classical text (*charak samhita* and

commentaries) along with research journals and magazines are reviewed to collect the data during work. Also websites like pubmed, google scholar and Wikipedia were used.

METHODS-Literary data collected was compared and analysed on classical background to find similarities and dissimilarities and clinical approach in accordance to modern sciences.

4. EPIGENETICS AND INFERTILITY

EPIGENETICS- Epi-greek=on the top, over. This process induces change in phenotype without the change in basic constitution of genes i.e. genotype.^[9]

The process of modifying DNA expression includes.

- 1) DNA Methylation,
- 2) Histone Modification,
- 3) Chromatin remodeling,
- 4) Micro RNA(miRNA)

1) DNA Methylation-Methyl groups are added to DNA molecules. This is called as DNA methylation and it makes changes in DNA expression.^[10]

2) Histone modification-Histones are proteins that DNA wraps around the nucleus forming chromatin. It makes the DNA more compact and protects its structure.^[11]

3) Chromatin remodeling-Chromatin is complex of proteins and DNA is tightly bundled to fit into the nucleus. There is modification in chromatin structure to influence the gene expression. Tightly folded chromatin tends to shut down while more open chromatin is functional and are expressed.^[10]

4) Micro RNA-Micro RNA refers to small non coding RNA molecules that stops the function of m-RNA.^[12]

INFERTILITY

Infertility is defined as a failure to conceive within one or more years of regular unprotected coitus.^[13] Amongst the thousands of reasons for infertility, excluding the anatomical defects, the rest of reasons of infertility like anovulation, repeated abortions, congenital malformations of the fetus, hormonal imbalance are associated with epigenetic changes.

This new concept of epigenetics simply tries to answer to the most unexplained causes of infertility and there are numerous studies which show the relation between epigenetics and infertility. This article tries to focus on 4 main causes of infertility i.e. 1) diet 2) environmental

changes 3) night shifts 4) stress.

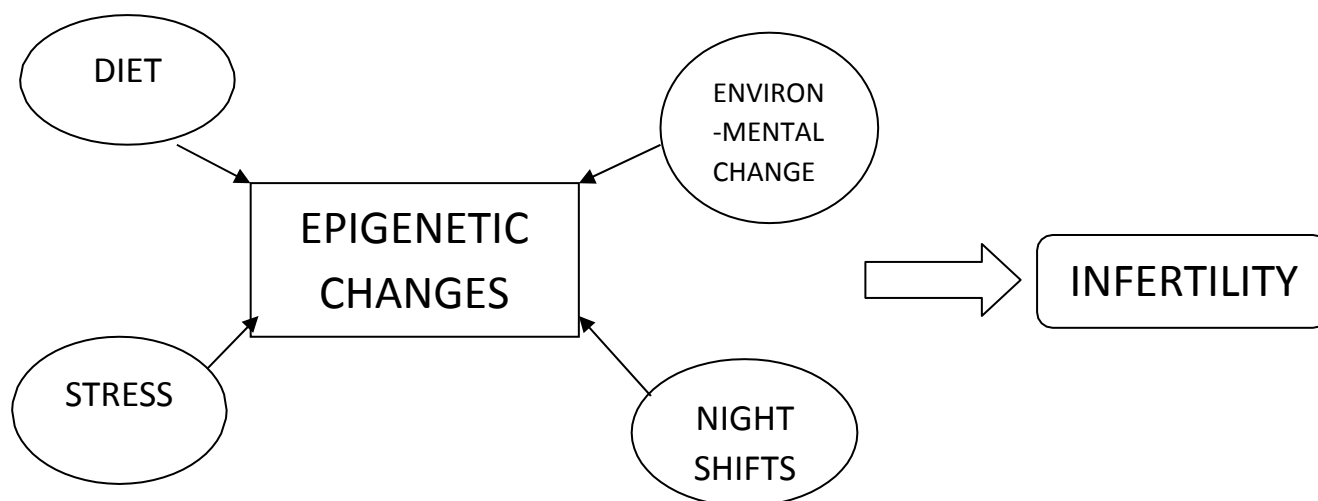


FIG 1: Factors causing epigenetic changes.

5. AIMS AND OBJECTIVES

- 1) To review epigenetics and infertility from different books, research articles and websites.
- 2) To find the relevant data described in ayurveda.
- 3) To find out solutions mentioned in ayurveda on infertility related factors.

6. FACTORS

6.1) DIET- Eating junk food, food with added preservatives, stale food, packaged food with artificial flavour do have a effect on the body along with the genes. Diet can modify mechanisms by regulating DNA methylation, Histone modification, chromatin remodeling and miRNA expression.^[14, 15]

The modern day sedentary life style have led us to verociously increasing threat of obesity where studies show that women have higher obesity rates than men.^[16] Obesity is defined as excessive body fat having BMI greater than 25.^[17] Obesity is regarded as a disrupter of female fertility. Increased BMI is associated with ovulatory sub fertility and anovulatory infertility.^[18] Even obesity disturbs the hormonal balance of women which directly affects her fertility.^[19]

While the modern science describes ‘epigenetics diet’ for the cure if epigenetic aberrations as treatment for cancer, ancient ayurveda has already described the concept of *Ashtau-Ahar-Vidhi-Vishesh-Ayatane*^[20] along with diet according to *Ritu*.

6.2) ENVIRONMENTAL CHANGES

Environment significantly affects female fertility.^[4] Increased industrialization, number of vehicles, fumes, exhaust from chemical factories have led to drastic changes in environment which directly and indirectly affect the fertility in women.^[13]

Environmental toxicants and environmental stress can promote epigenetic alterations that are transmitted to subsequent generations, resulting in disease.^[21] Exposure to air pollution during gestation affects gestating mother, her embryo and its developing germline thereby influencing third generations phenotype.^[22]

The main air contaminants appear to impair both animal and human gametogenesis and lead to a drop in reproductive performance.^[23, 24]

Several reports have claimed that women living in highly industrialized areas have fewer fertilizable oocytes due to significant decrease in antral follicle number to a lower fertility rate and to a higher implantation failure rate in comparison with controls.^[23, 24] Santi *et al.* assessed the correlation between increased air pollution and decreased fertility by determining serum AMH levels.

Low levels of reactive oxygen species stimulate cell recovery/survival and high levels alter epigenetic mechanisms and induce degenerative process via activation of p53 and pro-apoptotic genes.^[4]

6.3) Night Shifts

A recent study shows that more than 15% of population is working in night shifts today and 24% fear insomnia.^[25] Working in night shifts has now become a part of our new generation life style and somehow it is necessary so as to earn a penny. Night shifts affect the whole physical and mental well being of the person disturbing his biological clock. The regular rhythms of sleep and diet get terrifically affected.

It has been identified that working in night shifts modify epigenetic patterns.^[26] Several epidemiological studies show that working in night shifts alter DNA methylation including changes in gene specific methylation of inflammatory genes.^[26]

This sub topic not only includes working in night shifts but also specifically includes staying awake till late night which is the most popular trend amongst the young nowadays. Staying

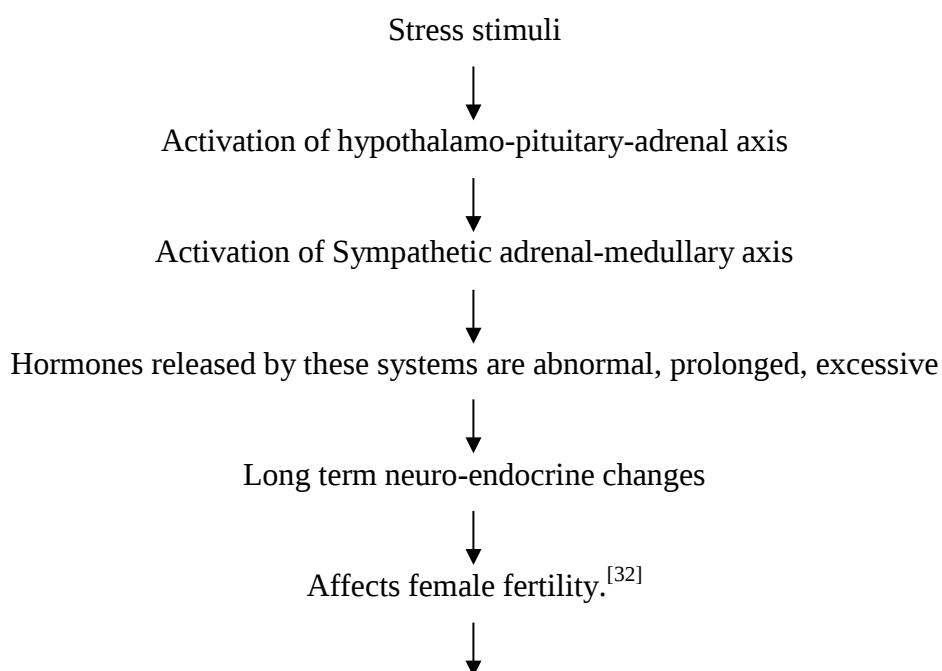
awake late night has the same effects like working in night shifts.

Night shift work for women causes menstrual irregularity, endometriosis and prolonged time of conception. Among women ≤ 35 years night workers were more likely to require fertility treatment.^[27] A third of women who worked night shifts had an increased rates of miscarriage.^[28]

6.4) STRESS- Exposure to stressors change epigenetic marks or tags and influence the way genes are expressed.^[29]

122 women were interviewed prior to their first infertility clinic visit and 40% of women were having anxiety with depression. The same study also concluded that out of 106 women 9.4% women had suicidal attempts.^[30]

Now a confirmed relation is established between female body stress response and hormone involvement.^[31]



Psychological interventions are necessary for women with infertility and they have potential to decrease anxiety and depression and led to increased pregnancy rates.^[33]

7. DISCUSSION

The 4 main external factors of infertility in females discussed above have an answer in our *samhitas*. These epigenetic changes are reversible.^[14] Hence just accepting small

modifications in day to day life can bring our genes back to normal. Having food as described in *Ashtau-Ahar-Vidhi-Vishesh-Ayatane*, diet according to *Ritu*, diet according to *Prakruti* of an individual can help keep one's health better.

Regarding the stress factors, meditation, *dhyan* described in *Swasthavritta* helps reduce the stressors. Research has demonstrated the health benefits of this type of meditation.^[34] Even the concept of *Sadvritta* has a major impact on one's behavior – indirectly acting upon the genes.

Although major factors of the environment can't be avoided but some initiative can be taken towards reducing these factors. Living in pollution free environment, breathing exercises(*Pranayam*), avoiding exposure to fumes and carbon particles can be done.

A study on the impact of health promoting intervention that included increased physical activity and increased intake of fruits and vegetables impacted patterns of DNA methylation in gene regions related to immune cell metabolism, tumor suppression and overall aging.^[35] Studies have shown correlation between exercise and DNA methylation with concordant health changing the phenotype.^[36]

All the above discussions suggest that Ayurveda is the answer for epigenetic changes and female infertility.

8. CONCLUSION

From all the above data and discussions, it is clear that epigenetics in hundreds of ways affects the female fertility and ayurveda in thousands of ways have the cure for it.

Ayurveda follows natural ways of healing and prevention of disease before the disease actually manifests. The epigenetic changes due to modern life style can be reversed by following the basic rules of ayurveda which our *Acharyas* have discussed ages ago. Studies have shown factors that cause epigenetic changes affect DNA expression and this can be transmitted to the progeny causing birth defects as well.^[21] Thus this is an alarming sign that our future generations are also at a risk. Hence it is proposed that epigenetics is an important mechanism of Ayurveda.^[37]

In order to reduce the health risks for the offsprings it is recommended to optimize the oxidative, epigenetic situation of females by means of lifestyle adaptation and use of

appropriate food supplementation before conception.

This correlation of ayurveda and epigenetics can lead to better integration of both the sciences giving the best health results where ancient wisdom and modern knowledge will go hand in hand and bring to the world the best progeny.

9. REFERENCES

1. www.google.com-definitions from oxford languages.
2. Charak samhita-Dr.Bramhanad Tripathi-published by choukhamba surbharti Varanasi in Indriya sthan adhaya 1 varnaswarendriya adhyaya shloka no.5.
3. Belen Hurrel, PhD Epigenetics:National Human genome research institute, ss December 8, 2022.
4. Rita canipari, lucia De Santis, sundra Cecconi-Female Fertility and environmental pollution. 26 nov 2020-[google scholar].
5. Charak samhita-Dr.Bramhanad Tripathi-published by choukhamba surbharti Varanasi sharir sthan adhaya 4 Mahatigarbhavkranti adhyaya shloka no.6.
6. Charak samhita-Dr.Bramhanad Tripathi-published by choukhamba surbharti Varanasi sharir sthan adhaya 4 Mahatigarbhavkranti adhyaya shloka no.5.
7. Govindaraj, P.; Nizamuddin, S.; Sharath, A.; Jyothi, V.; Rotti, H.; Raval, R.; Nayak, J.; Bhat, B.K.; Prasanna, B.V.; Shintre, P.; et al. Genome-wide Analysis Correlates Ayurveda Prakriti. *Sci.Rep*, 2015; 5: 15786.[CrossRef] [PubMed]
8. Patwardhan, B.; Joshi, K.; Chopra, A. Classification of Human Population Based on HLA Gene Polymorphism and the Concept of Prakriti in Ayurveda. *J. Altern. Complement. Med*, 2005; 11: 349–353.
9. www.wikipedia.com.
10. Epigenetics: the science of change-Bob weinhold, Environmental health perspectives National institute of Environmental health science March, 2006.
11. Fan, J.; Krautkramer, K.A.; Feldman, J.L.; Denu, J.M. Metabolic Regulation of Histone Post-translational Modifications. *ACS Chem. Biol*, 2015; 10: 95–108.
12. Lu, T.X.; Rothenberg, M.E. MicroRNA. *J. Allergy Clin. Immunol*, 2018; 141: 1202–1207.
13. DC Dutta text book of gynecology by Hiralal konar-Infertility lesson page no, 217.
14. Abdul, Q.A.; Yu, B.P.; Chung, H.Y.; Jung, H.A.; Choi, J.S. Epigenetic Modifications of Gene Expression by Lifestyle and Environment. *Arch. Pharm. Res*, 2017; 40: 1219–1237.

15. Choi, S.-W.; Friso, S. Epigenetics: A New Bridge Between Nutrition and Health. *Adv. Nutr.* 2010; 1: 8.
16. Unicef's World obesity atlas 2022, 29 July, 2022(17)www.wikipedia.com-obesity
- 17 Shilpa pandey, suruchi Pandey, Siladitya Bhattacharya-The impact of female obesity on the outcome of fertility treatment- *Journal of Human Reproductive Sciences*, 2010 May-August; 3(2): 62-67.
- 18 Bhavana seth, Sarika arora, Ritu singh-Association of obesity with hormonal imbalance in infertility; A cross sectional study of North Indian women; *Indian journal of clinical Biochemistry*.
17. Charak samhita-Dr.Bramhanad Tripathi-published by choukhamba surbharti Varanasi viman sthan adhaya 1Rasvimaniya adhyaya shlok no.21.
18. Skinner, M.K. Environmental Stress and Epigenetic Transgenerational Inheritance. *BMC Med*, 2014; 12: 153.
19. Shukla, A.; Bunkar, N.; Kumar, R.; Bhargava, A.; Tiwari, R.; Chaudhury, K.; Goryacheva, I.Y.; Mishra, P.K.-Air Pollution Associated Epigenetic Modifications: Transgenerational Inheritance and Underlying Molecular Mechanisms. *Sci. Total Environ*, 2019; 656: 760–777.
20. Does air pollution play a role in infertility?; A systematic review. *Environmental health*, 2017; 16: 1-16 [google scholar].
21. Conforti.A; Mascia M, Cioffi G.d, Angelis-Air pollution and female fertility: A systematic review of literature, 2018; 16: 117, google scholar.
22. The economic times-By Glynda Alves, Et Bureau, May 04, 2021.
23. Alegria-Torres, J.A.; Baccarelli, A.; Bollati, V. Epigenetics and Lifestyle. *Epigenomics*, 2011; 3: 267–277. [PubMed]
24. Renac.c, Fernandez, Vivienne M.Moore and Michel J.Davies-Night shift among women: is it associated with difficulty in conceiving a first birth?-*Occupational Health and safety*.
25. Katieforster-Shift work and heavy lifting may reduce women's fertility-independebt.co.uk
26. Zannas, A.S.; West, A.E. Epigenetics and the Regulation of Stress Vulnerability and Resilience. *Neuroscience*, 2014; 264: 157–170. [PubMed]
27. Shani.c, Yelena.s-Suicidal risk among infertile women undergoing IVF: incidence and risk factors, 2016; 240: 53-59 [pubmed], [google scholar].
28. Whirledge S, Cidlowski JA-Glucocorticoids, stress and infertility: *Minerva Endocrinol*, 2010; 35: 109-125.
29. Schenker JG, Meirow D, Schenker E-Stress human reproduction *Eur J-Obstet*

- GynecologyReprod Biol, 1992; 16: 1-8 [pubmed] [google scholar]
30. Kristin Rooney, BA and Alice D.DomwAr-The relationship between stress and infertility-Dialogues in clinical neuroscience, March 2018.
 31. Sharma, H. Meditation: Process and effects. AYU, 2015; 36: 233–237.
 32. Hibler, E.; Huang, L.; Andrade, J.; Spring, B. Impact of a Diet and Activity Health Promotion Intervention on Regional Patterns of DNA Methylation. Clin. Epigenetics, 2019; 11: 133.
 33. Rönn, T.; Volkov, P.; Davegårdh, C.; Dayeh, T.; Hall, E.; Olsson, A.H.; Nilsson, E.; Tornberg, A.; Nitert, M.D.; Eriksson, K.-F.; et al. A Six Months Exercise Intervention Influences the Genome-wide DNA Methylation Pattern in Human Adipose Tissue. PLoS Genet, 2013; 9.
 34. Hari Sharma and Robert keith Wallace-Ayurveda and Epigenetics –medicina, 2020 dec 11.
 35. FH Corraire, W Vandeberghe and WAE Declear-External factors addecting fertility andhow to correct their impact-Facts views via Obgy, 2017 Dec 9: 217-221.