ejpmr, 2021,8(1), 253-258

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

CRITICAL REVIEW OF *VYADHIKSHAMATVA* WITH ROLE OF THYMUS GLAND IN HUMAN IMMUNE SYSTEM

Dr. Gurunath Digambar Khanolkar[1], Dr. Suryakant D. Rokade[2*] and Dr. Somya O. Singh[3]

[1]Associate Professor, Department of Rachna Sharir, R. A Podar Medical College, Worli Maharashtra-400018.
[2]Head of Department of Rachna Sharir, Govt. Ayurveda College, Nanded, Maharashtra-431601.
[3]PG Student, Department of Rachna Sharir, Govt. Ayurveda College, Nanded, Maharashtra-431601.

***Corresponding Author: Dr. Suryakant D. Rokade**

Head of Department of Rachna Sharir, Govt. Ayurveda College, Nanded, Maharashtra-431601.

Article Received on 13/11/2020 **Article Revised on 03/12/2020** **Article Accepted on 23/12/2020**

ABSTRACT

Ayurveda propounds that prevention is an equally important aspect of disease management as cure and thus, strengthening the immune system, is a natural way to help the body fight against the disease-causing pathogens). Changing demographic profile, changing climate, lot of stress work all these causes many harmful diseases. The body's resistance is of tremendous importance in the daily welfare of living beings not only for disease prevention but also for rapid recovery after disease affliction. The fundamental principle of Ayurveda is unchangeable and unaffected by winds of doctrines, one of such fundamental principles of, one of such fundamental principles of Ayurveda is *Vyadhikshamatva* (Immunity*)*. Human immune system is a complex network of cells, tissues, and organs. It's a bodily system that protects the body from foreign substances, cells, and tissues by producing the immune response and that includes especially the thymus, spleen, lymph nodes, special deposits of lymphoid tissue (as in gastrointestinal tract and bone marrow), macrophages, lymphocytes including the B cells band T cells, and antibodies. Thymus gland is an organ that is critically important to the immune system which serves as the body's defense mechanism providing surveillance and protection against diverse pathogens, tumors, antigens and mediators of tissue damage.

KEYWORDS: Ayurveda, *Vyadhiksthamatva.*

INTRODUCTION

The science of Ayurveda is not only holding within it the measures for alleviation from discomforts but its foremost aim is the maintenance of homeostasis and better approach towards healthy and happy life. Advances in the field of environmental health have taught us much about human health hazards; for example, air pollution can cause respiratory disease, heavy metals can cause neurotoxicity, global climate change is likely to fuel the spread of infectious diseases. The nature has made the natural safety measures to claim superiority over such natural influences that hamper life. The nature had given us power to adapt and overcome these variations. This adaptability of the body is termed as *Vyadhikshamatva*. In terms of medical science, it is called immunity.

Concept of *Vyadhikshamatva*

The main purpose and objectives of Ayurveda is the preservation of health in healthy individual and eradication of diseases which are curable.[1] Ayurveda emphasizes the promotion of health through the strengthening of host defenses to act as a resistive force against day to day physiological extremes as well as opportunistic maladies. This force to reckon with, as regards everyday wellness is termed as *'Vyadhikshamtva'* in Ayurveda.

The term *Vyadhikshamatva* is made up of two words;

1) ***Vyadhi*****:** means 'to harm', 'to injure', 'to damage' or 'to hurt'.

2) ***Kshamatva*****:** means 'to compose', 'to suppress anger' or 'keep quite or to resist'.

Vyadhi is a condition which comes into existence as consequence of non- equilibrium of the *doshas* (physiological factors that is *Vata*, *Pitta*, and *Kapha*), *dhatus* (tissue systems) and *malas* (excretory products of body) which in their normal status maintains the physical and physiological health). The word *Kshamatva* is derived from '*Kshamus Sahane'* meaning there by to be patient or composed or to resist. So, *Vyadhikshamtva* is that factor which limits the pathogenesis and opposes the strength of diseases. *Vyadhikshamatva* was first defined by Chakrapani in a very scientific manner in terms of *'Vyadhi-balavirodhitvam'* capacity of the body to not allow to produce disease or pathogenesis. It denotes the resistance power of the body/defense of the body against first occurrence of any disease. Also, in second term it indicates that if body once is being encountered by some disease it will not allow the disease to be manifested because of possessing a specific resistance power Synonyms of *Vyadhikshamatva*: *Sleshma*, *Bala*, *Ojas*.

Ojas and Bala

Ojas is defined as the final and excellent essence of *Saptadhatus* beginning with *rasa* and ending with *shukra dhatu*. *Ojas* of the body is situated in heart and is white, yellowish and reddish in colour, or color of ghee, taste like Honey and smell like fried paddy.[2] *Acharya Charak* says that *Ojas* is *Pranayatan*[3] means, if *Ojas* is destroyed, the human being also perishes. Properties of *Ojas* are *Guru* (heavy), *Sheet* (cool), *Mrudu* (soft) the *Slakshna* (smooth), *Bahal* (dense), *Madhura* (sweet), *Sthira* (responsible for stability), *Prasnna* (clear), *Picchila* (slimy) and *Snigdha* (unctuous). According to *Chakrapani Ojas* is of two types;[4]

- ***Para Ojas*: *Para Ojas*** is prime *Ojas*, where *Prana* the life resides. It is 8 drops in quantity, present in heart, even a part of destruction of *Para Ojas* leads to death. It is white and Yellowish red in colour.
- ***Apara Ojas***: *Apara Ojas* is half Anjali in quantity, it is less important compared to *Para Ojas*.

The term *Bala* are used as synonyms of *Ojas*. The *Bala* signifies the physical, mental strength of body resistance. *Bala* has been classified into three types as;

- *Sahaja bala*.
- *Kalaja bala*.
- *Yuktikruta bala*.

Sahaja bala is both mental and physical strength present naturally by birth. *Kalaja bala* is strength due to favorable conditions like youth, season and *Yuktikruta bala* is strength acquired by the intake of diet such as flesh, ghee etc. and by proper exercise. *Bala* is a multidimensional functional identity of the body, which is the output of proper equilibrium state of doshas, dhatu and mala in the body. This comes in the form of *Ojas* which is considered as the supreme essence of all the seven *rasadi dhatus*. It is also stated as *Sarvadhatusara*. In this manner *Ojas* is formed in our body which is the purest of all the *dhatus*. The expression of this supreme essence in the body results in the good musculature, stable body, ability to perform activities, clarity of voice, good complexion, healthy *Karmendriyas* (motor organs and nerves) and *Gyanendriyas* (sensory organs and nerves) and healthy *Vyadhikshamatva* (immunity power) of body, all these features are related to *bala*. Hence it is to be said that Bala is the *Karya* (action) and *Ojas* is the *Karan* (cause) for *Bala*.

Relation between *Vyadhikshamatva*, *Bala* and *Ojas*

Bala is the cause for the good defense mechanism and to carry out all the physical and psychological actions. The depreciation of *Bala* is a constant sign observed in various degenerative diseases and recurrent infections. It can be increased by intake of wholesome food, immunomodulator drugs like Tinospora Cordifolia Wild. (family- Menispermaceae) etc., a regular routine of seasonal and daily regimens along with mild physical workout. So, *Bala* and *Vyadhikshamatva* have cause and effect relationship. In Ayurveda, the superior vital essence of all bodily tissues is called "*Ojas*". Overall it is responsible for the defense of human body against diseases and infirmity. In conditions like diabetes mellitus, immunodeficiency disorders and malnutrition, where loss of ojas or bala is a constant feature, people are known to be susceptible to various other diseases or recurrent infections. According to the concept of *Ojas* or *Vyadhikshamatva* or *Bala* (immunity), the body's resistance is of tremendous importance in the daily welfare of living beings not only for disease prevention but also for rapid recovery after disease affliction. *Ojas* is responsible for good health, better immunity, longevity, intelligence and thought process.

DISSCUSION

Human Immune System

Human immune system is a complex network of cells, tissues, and organs. It's a bodily system that protects the body from foreign substances, cells, and tissues by producing the immune response and that includes especially the thymus, spleen, lymph nodes, special deposits of lymphoid tissue (as in gastrointestinal tract and bone marrow), macrophages, lymphocytes including the B cells band T cells, and antibodies.

Components of human immune system

The immune system protects its host from infection with layered defenses of increasing specificity in the form of;

- Innate immune system
- Adaptive immune system

Innate immune system

Microorganisms or toxins that successfully enter an organism encounter the cells and mechanisms of the innate immune system. The innate response is usually triggered when microbes are identified by pattern recognition receptors, which recognize components that are conserved among broad groups of microorganisms, or when damaged, injured or stressed cells send out alarm signals, many of which are recognized by the same receptors as those that recognize pathogens. Innate immune defences are non-specific, meaning these systems respond to pathogens in a generic way. This system does not confer long-lasting immunity against a pathogen. The innate immune system is the dominant system of host defence in most organisms.

Adaptive immune system

The adaptive immune system evolved in early vertebrates and allows for a stronger immune response as well as immunological memory, where each pathogen is "remembered" by a signature antigen. The adaptive immune response is antigen-specific and requires the recognition of specific "non-self" antigens during a process called antigen presentation. Antigen specificity allows for the generation of responses that are tailored to specific pathogens or pathogen-infected cells. The ability to mount these tailored responses is maintained in the body by "memory cells". Should a pathogen infect the body more than once, these specific memory cells are used to quickly eliminate it.

Thymus gland

The thymus is a specialized primary lymphoid organ of the immune system. Within the thymus, Thymus cell lymphocytes or T cells mature. T cells are critical to the adaptive immune system, where the body adapts specifically to foreign invaders. The thymus is located in the upper front part of the chest, in the anterior superior mediastinum, behind the sternum, and in front of the heart. It is made up of two lobes, each consisting of a central medulla and an outer cortex, surrounded by a capsule. The thymus is made up of immature T cells called thymocytes, as well as lining cells called epithelial cells which help the thymocytes develop. T cells that successfully develop react appropriately with MHC immune receptors of the body (called positive selection,) and not against proteins of the body, (called negative selection). The thymus is largest and most active during the neonatal and pre-adolescent periods. By the early teens, the thymus begins to decrease in size and activity and the tissue of the thymus is gradually replaced by fatty tissue. Nevertheless, some T cell development continues throughout adult life. Abnormalities of the thymus can result in a decreased number of T cells and autoimmune diseases such as Autoimmune polyendocrine syndrome type 1 and myasthenia gravis. These are often associated with cancer of the tissue of the thymus, called thymoma, or tissues arising from immature lymphocytes such as T cells, called lymphoma. Removal of the thymus is called thymectomy.

Anatomy of Thymus gland

The thymus is an organ that sits beneath the sternum in the upper front part of the chest, stretching upwards towards the neck. In children, the thymus is pinkish-gray, soft, and lobulated on its surfaces. At birth it is about 4–6 cm long, 2.5–5 cm wide, and about 1 cm thick. It increases in size until puberty, where it may have a size of about 40–50 g, following which it decreases in size in a process known as involution.

The thymus is made up of two lobes that meet in the upper midline, and stretch from below the thyroid in the neck to as low as the cartilage of the fourth rib. The lobes are covered by a capsule. The thymus lies beneath the sternum, rests on the pericardium, and is separated from the aortic arch and great vessels by a layer of fascia. The left brachiocephalic vein may even be embedded within the thymus. In the neck, it lies on the front and sides of the trachea, behind the sternohyoid and sternothyroid muscles.

Microanatomy

The thymus consists of two lobes, merged in the middle, surrounded by a capsule that extends with blood vessels into the interior. The lobes consist of an outer cortex rich with cells and an inner less dense medulla. The lobes are divided into smaller lobules 0.5-2mm diameter, between which extrude radiating insertions from the capsule along septa. The cortex is mainly made up of thymocytes and epithelial cells. The thymocytes, immature T cells, are supported by a network of the finely-branched epithelial reticular cells, which is continuous with a similar network in the medulla. This network forms an adventitia to the blood vessels, which enter the cortex via septa near the junction with the medulla. Other cells are also present in the thymus, including macrophages, dendritic cells, and a small amount of B cells, neutrophils and eosinophils.

In the medulla, the network of epithelial cells is coarser than in the cortex, and the lymphoid cells are relatively fewer in number. Concentric, nest-like bodies called Hassall's corpuscles (also called thymic corpuscles) are formed by aggregations of the medullary epithelial cells. These are concentric, layered whorls of epithelial cells that increase in number throughout life. They are the remains of the epithelial tubes, which grow out from the third pharyngeal pouches of the embryo to form the thymus.

Blood and nerve supply

The arteries supplying the thymus are branches of the internal thoracic, and inferior thyroid arteries, with branches from the superior thyroid artery sometimes seen. The branches reach the thymus and travel with the septa of the capsule into the area between the cortex and medulla, where they enter the thymus itself; or alternatively directly enter the capsule. The veins of the thymus end in the left brachiocephalic vein, internal thoracic vein, and in the inferior thyroid veins. Sometimes the veins end directly in the superior vena cava. Lymphatic vessels travel only away from the thymus, accompanying the arteries and veins. These drain into the brachiocephalic, tracheobronchial and parasternal lymph nodes. The nerves supplying the thymus arise from the Vagus nerve and the cervical sympathetic chain. Branches from the phrenic nerves reach the capsule of the thymus, but do not enter into the thymus itself.

Development

The thymocytes and the epithelium of the thymus have different developmental origins. The epithelium of the thymus develops first, appearing as two outgrowths, one on either side, of the third pharyngeal pouch. It sometimes also involves the fourth pharyngeal pouch. These extend outward and backward into the surrounding mesoderm and neural crest-derived mesenchyme in front of the ventral aorta. Here the thymocytes and epithelium meet and join with connective tissue. The pharyngeal opening of each diverticulum is soon obliterated, but the neck of the flask persists for some time as a cellular cord. By further proliferation of the cells lining the flask, buds of cells are formed, which become surrounded and isolated by the invading mesoderm. The epithelium forms fine lobules, and develops into a sponge-like structure. During this stage, hematopoietic bone-marrow precursors migrate into the thymus. Normal development is dependent on the interaction between the epithelium and the hematopoietic thymocytes. Iodine is also necessary for thymus development and activity.

Involution

The thymus continues to grow after the birth reaching the relative maximum size by puberty. It is most active in fetal and neonatal life. It increases to 20 - 50 grams by puberty. It then begins to decrease in size and activity in a process called thymic involution. After the first year of life the amount of T cells produced begins to fall. Fat and connective tissue fills a part of the thymic volume. During involution, the thymus decreases in size and activity. Fat cells are present at birth, but increase in size and number markedly after puberty, invading the gland from the walls between the lobules first, then into the cortex and medulla. This process continues into old age, where whether with a microscope or with the human eye, the thymus may be difficult to detect, although typically weights 5 - 15 grams. The atrophy is due to the increased circulating level of sex hormones, and chemical or physical castration of an adult results in the thymus increasing in size and activity. Severe illness or human immunodeficiency virus infection may also result in involution.

Role of Thymus gland in Human immune system

T cell maturation

The thymus facilitates the maturation of T cells, an important part of the immune system providing cell-mediated immunity. T cells begin as hematopoietic precursors from the bone-marrow, and migrate to the thymus, where they are referred to as thymocytes. In the thymus they undergo a process of maturation, which involves ensuring the cells react against antigens ("positive selection"), but that they do not react against antigens found on body tissue ("negative selection"). Once mature, T cells emigrate from the thymus to provide vital functions in the immune system. Each T cell has a distinct T cell receptor, suited to a specific substance, called an antigen. Most T cell receptors bind to the major histocompatibility complex on cells of the body. The MHC presents an antigen to the T cell receptor, which becomes active if this matches the specific T cell receptor. In order to be properly functional, a mature T cell needs to be able to bind to the MHC molecule ("positive selection"), and not to react against antigens that are actually from the tissues of body ("negative selection"). Positive selection occurs in the cortex and negative selection occurs in the medulla of the thymus. After this process T cells that have survived leave the thymus, regulated by sphingosine-1-phosphate. Further maturation occurs in the peripheral circulation. Some of this is because of hormones and cytokines secreted by cells within the thymus, including thymulin, thymopoietin, and thymosins.

Clinical significance

Immunodeficiency

As the thymus is where T cells develop, congenital problems with the development of the thymus can lead to immunodeficiency, whether because of a problem with the development of the thymus gland, or a problem specific to thymocyte development. Immunodeficiency can be profound. Loss of the thymus at an early age through genetic mutation as in DiGeorge syndrome, CHARGE syndrome, or a very rare "nude" thymus causing absence of hair and the thymus results in severe immunodeficiency and subsequent high susceptibility to infection by viruses, protozoa, and fungi.

The most common congenital cause of thymus-related immune deficiency results from the deletion of the 22nd chromosome, called DiGeorge syndrome. This results in a failure of development of the third and fourth pharyngeal pouches, resulting in failure of development of the thymus, and variable other associated problems, such as congenital heart disease, and abnormalities of mouth (such as cleft palate and cleft lip), failure of development of the parathyroid glands, and the presence of a fistula between the trachea and the esophagus. Very low numbers of circulating T cells are seen. The condition is diagnosed by fluorescent in situ hybridization and treated with thymus transplantation.

Severe combined immunodeficiency (SCID) are group of rare congenital genetic diseases that can result in combined T, B, and NK cell deficiencies. These syndromes are caused by mutations that affect the maturation of the hematopoietic progenitor cells, which are the precursors of both B and T cells. A number of genetic defects can cause SCID, including IL-2 receptor gene loss of function, and mutation resulting in deficiency of the enzyme adenine deaminase.

Autoimmune disease

Autoimmune polyendocrine syndrome

Autoimmune polyendocrine syndrome type 1, is a rare genetic autoimmune syndrome that results from a genetic defect of the thymus tissues. Specifically, the disease results from defects in the autoimmune regulator (AIRE) gene, which stimulates expression of self-antigens in the epithelial cells within the medulla of the thymus. Because of defects in this condition, self-antigens are not expressed, resulting in T cells that are not conditioned to tolerate tissues of the body, and may treat them as foreign, stimulating an immune response and resulting in autoimmunity.

Thymoma-associated multiorgan autoimmunity

Thymoma-associated multiorgan autoimmunity can occur in people with thymoma. In this condition, the T cells developed in the thymus are directed against the tissues of the body. This is because the malignant thymus is incapable of appropriately educating developing thymocytes to eliminate self-reactive T cells. The condition is virtually indistinguishable from graft versus host disease.

Myasthenia gravis

Myasthenia gravis is an autoimmune disease most often due to antibodies that block acetylcholine receptors, involved in signaling between nerves and muscles. It is often associated with thymic hyperplasia or thymoma, with antibodies produced probably because of T cells that develop abnormally. Myasthenia gravis most often develops between young and middle age, causing easy fatiguing of muscle movements. Investigations include demonstrating antibodies (such as against acetylcholine receptors or muscle-specific kinase), and CT scan to detect thymoma or thymectomy. With regard to the thymus, removal of the thymus, called thymectomy may be considered as a treatment, particularly if a thymoma is found. Other treatments include increasing the duration of acetylcholine action at nerve synapses by decreasing the rate of breakdown. This is done by acetylcholinesterase inhibitors such as pyridostigmine.

Cancer: Tumors of the hematopoietic and lymphoid tissues

Thymomas

Tumors originating from the thymic epithelial cells are called thymomas. They most often occur in adults older than 40. Tumors are generally detected when they cause symptoms, such as a neck mass or affecting nearby structures such as the superior vena cava; detected because of screening in patients with myasthenia gravis, which has a strong association with thymomas and hyperplasia; and detected as an incidental finding on imaging such as chest x-rays. Hyperplasia and tumors originating from the thymus are associated with other autoimmune diseases - such as hypogammaglobulinemia, Graves' disease, pure red cell aplasia, pernicious anemia and dermatomyositis, likely because of defects in negative selection in proliferating T cells.

Lymphomas

Tumors originating from T cells of the thymus form a subset of acute lymphoblastic leukemia (ALL). These are similar in symptoms, investigation approach and management to other forms of ALL. Symptoms that develop, like other forms of ALL, relate to deficiency of platelets, resulting in bruising or bleeding; immunosuppression resulting in infections; or infiltration by cells into parts of the body, resulting in an enlarged liver, spleen, lymph nodes or other sites. Blood test might reveal a large amount of white blood cells or lymphoblasts, and deficiency in other cell lines - such as low platelets or anemia. Immunophenotyping will reveal cells that are CD3, a protein found on T cells, and help further distinguish the maturity of the T cells. Genetic analysis including karyotyping may reveal specific abnormalities that may influence prognosis or treatment, such as the Philadelphia translocation. Management can include multiple courses of chemotherapy, stem cell transplant, and management of associated problems, such as treatment of infections with antibiotics, and blood transfusions. Very high white cell counts may also require cytoreduction with apheresis.

Tumors originating from the small population of B cells present in the thymus lead to primary mediastinal (thymic) large B cell lymphomas. These are a rare subtype of Non-Hodgkin's lymphoma, although by the activity of genes and occasionally microscopic shape, unusually they also have the characteristics of Hodgkin's lymphomas. That occur most commonly in young and middle-aged, more prominent in females. Most often, when symptoms occur it is because of compression of structures near the thymus, such as the superior vena cava or the upper respiratory tract; when lymph nodes are affected it is often in the mediastinum and neck groups.

Thymic cysts

Cervical thymic cyst

The thymus may contain cysts, usually less than 4 cm in diameter. Thymic cysts are usuallydetected incidentally and do not generally cause symptoms. Thymic cysts can occur along the neck or in the chest (mediastinum). Cysts usually just contain fluid and are lined by either many layers of flat cells or column-shaped cells. Despite this, the presence of a cyst can cause problems similar to those of thymomas, by compressing nearby structures, and some may contact internal walls and be difficult to distinguish from tumors. When cysts are found, investigation may include a workup for tumors, which may include CT or MRI scan of the area the cyst is suspected to be in.

Surgical removal

Thymectomy is the surgical removal of the thymus. The usual reason for removal is to gain access to the heart for surgery to correct congenital heart defects in the neonatal period. Other indications for thymectomy include the removal of thymomas and the treatment of myasthenia gravis. In neonates the relative size of the thymus obstructs surgical access to the heart and its surrounding vessels. Removal of the thymus in infancy results in often fatal immunodeficiency, because functional T cells have not developed. In older children and adults, which have a functioning lymphatic system with mature T cells also situated in other lymphoid organs, the effect is lesser, and limited to failure to mount immune responses against new antigens.

CONCLUSION

Lives embraces the states of health and disease. Ayurveda, the unbeaten science deals with these states of life. Ayurveda incorporates both the preventive and curative aspects of human ailments, promising it as a holistic science. This holistic approach of Ayurveda resembles to the entire function of *Vyadhikshamatva*. This can steer away the origin and or progression of various diseases. *Vyadhikshamatva* is a broad concept comprising the whole modern understanding of immunology and human body. The least understood arm of immunology is the origin and mechanism the development of auto-immune disorders.

REFERENCES

1. Acharya Vidhyadharshukla, Prof Ravidutt Tripathi, Charaksamhita of Agnivesa, Chaukhamba Sanskrit Prathisthan, Volume 1, Reprinted edition, 2015; 447.
2. Acharya Vidhyadharshukla, Prof Ravidutt Tripathi, Charaksamhita of Agnivesa, Chaukhamba Sanskrit Prathisthan, Volume 1, Reprinted edition, 2015; 267.
3. Acharya Vidhyadharshukla, Prof Ravidutt Tripathi, Charaksamhita of Agnivesa, Chaukhamba Sanskrit Prathisthan, Volume 1, Reprinted edition, 2015; 435.
4. Yadavji Trikamji and Nandkishor Sharma, Bhanumati Commentory by Chakrapanidatta on Sushrut Samhita, Sutrasthana, Krishnadas Academy, Varanasi Reprinted, 2001.
5. medlineplus.gov>Health Topic.
6. en.m.wikipedia.org>wiki>Immune system.
7. www.ncbi.nlm.nih.gov.