International Research Journal of Pharmacy and Medical Sciences
ISSN (Online): 2581-3277

Ciliary Dysfunction: The Root Cause of Kartagener's Syndrome

Shaik Parveen, P. Sanjana, N. Sharanya, D. Gowthami*
Malla Reddy College of Pharmacy, Maisammaguda, Dhulapally, Kompally(PO), Secunderabad-500100
Corresponding Author Email: gowthami.doguparthi2003@gmail.com
sanjanapilli52@gmail.com, sharanyanarala22@gmail.com, shaikparveenasma@gmail.com

Abstract*—Kartagener's syndrome (KS) is an uncommon genetic condition that follows an autosomal recessive pattern of inheritance and is marked by the three features of situs inversus, chronic sinusitis, and bronchiectasis. It is a subset of primary ciliary dyskinesia (PCD), resulting from mutations affecting the organization and role of motile cilia. Dysfunctional cilia impair mucociliary clearance impairment, resulting in recurrent respiratory infections, infertility, and other complications. Diagnosis is confirmed through clinical evaluation, genetic testing, and specialized tests like nasal nitric oxide measurement and electron microscopy of cilia. Management is symptomatic, focusing on respiratory therapy, antibiotics, and supportive care. Individuals who are affected can benefit from early diagnosis and intervention, as these can enhance their quality of life.*

***Keywords*—** *Kartagener's syndrome, situs inversus, primary ciliary dyskinesia, bronchiectasis, chronic sinusitis, ciliary dysfunction, genetic disorder.*

I. INTRODUCTION

A very rare genetic condition that affects individuals in an autosomal recessive manner cilia is Kartagener's Syndrome (1). The three conditions of situs inversus, chronic sinusitis and bronchiectasis (2) define this congenital deformity. In contrast to normal human anatomy, situs inversus is characterized by the organs in the chest and belly arranged in a mirror-image configuration. Chronic sinusitis is caused by ongoing inflammation and swelling of the sinuses, which are the cavities in the head and nose. Widening of the lungs' airways causes bronchiectasis, which increases the lungs' susceptibility to infection by causing an accumulation of extra mucus. Kartagener's Syndrome is a member of the category of PCDs known as ciliopathies. Impaired ciliary activity throughout the body is the result of this disorder (3). Either they don't move at all or they move incorrectly. Sperm cells, oviduct and bronchial epithelial cells, and ependymal cells lining brain vesicles are all impacted. Kartagener acknowledged the triad elements' causal link in 1933. Consanguineous marriages are more likely to experience this syndrome (4).

Cilia are the slender, thread-like extensions that stick out from the cell membrane. They perform a variety of biological tasks. Both sensitive and motile cilia are possible. Multiple ciliopathies are caused by primary flaws in their structure and process. Among them, Kartagener's Syndrome is the most notable. Cilia's main roles include protecting the lungs against the damaging impact of allergens, pollutants, and pathogens, as well as aiding mucociliary clearance, the upper respiratory tract's main innate defensive mechanism. Additionally, it facilitates the movement of mucus and other essential materials and is essential for the establishment and maintenance of the left-right axis throughout embryogenesis. It produces currents in the uterine tube lumen that drive the egg cell in the direction of the uterus, allowing fertilization to occur at the proper location (5). When cilia do not function properly, this leads to a build-up of mucus and bacterial colonization in the upper respiratory tract(4). Fig.1 illustrates the classic triad of Kartagener's Syndrome, comprising bronchiectasis, chronic sinusitis, and situs inversus with dextrocardia. This triad represents the hallmark clinical manifestations of the syndrome, with each component reflecting the underlying defect in ciliary structure and function. The interconnected nature of these symptoms emphasizes the systemic impact of impaired mucociliary clearance and embryonic development anomalies.

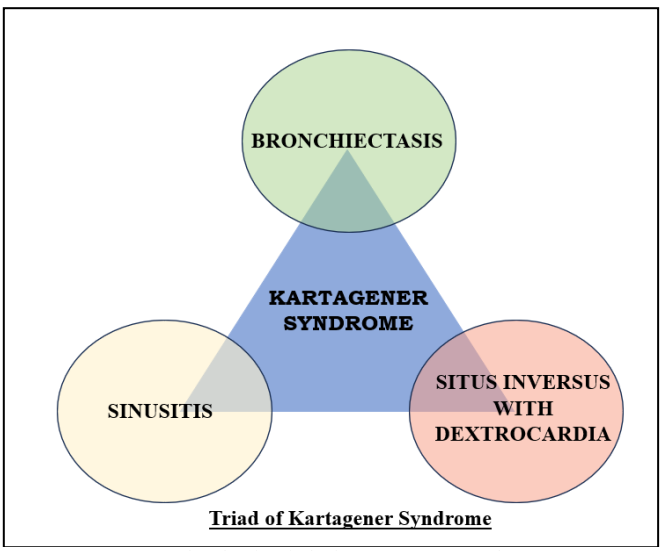

Fig. 1. The classic triad of Kartagener's Syndrome

Pathophysiology

1. *Defective Cilia Structure/Function:*
   - Cilia are crucial for removing mucus and debris from the respiratory tract, moving eggs through the fallopian tubes, and helping sperm swim.

Shaik Parveen, P. Sanjana, N. Sharanya, and D. Gowthami, "Ciliary Dysfunction: The Root Cause of Kartagener's Syndrome," *International Research Journal of Pharmacy and Medical Sciences (IRJPMS)*, Volume 8, Issue 2, pp. 52-55, 2025.

- In PCD, the cilia have structural abnormalities, like missing or defective dynein arms (proteins that help cilia move), leading to reduced or absent motility.

2. *Genetic Cause:*
   - It is inherited in an autosomal recessive pattern, meaning both parents must pass on the faulty gene.
3. *Kartagener's Syndrome (Subset of PCD):*
   - When PCD presents with situs inversus (organs reversed like a mirror image), chronic sinusitis, and bronchiectasis (permanent airway widening), it is called Kartagener's Syndrome.

Figure 2 provides a schematic overview of motile and non-motile cilia, highlighting their structural differences and functional roles. Motile cilia exhibit planar motion (9+2 microtubule arrangement) or rotary motion (9+0 arrangement), with examples including the cilia in the respiratory airways, fallopian tubes, sperm, and brain's ependymal cells. In contrast, non-motile cilia, also known as primary monocilia, are predominantly involved in sensory and signaling functions, as seen in kidney tubules, bile ducts, pancreatic ducts, and other tissues such as bones, cartilage, and photoreceptor cells in the eye.

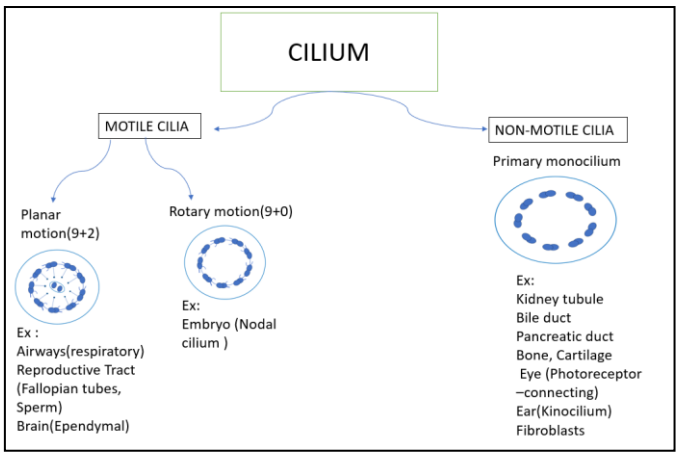

Fig. 2. A schematic overview of motile and non-motile cilia

Figure 3 depicts the ultrastructure of motile cilia, emphasizing its 9+2 microtubule arrangement. The diagram highlights key components, including the peripheral doublets, central microtubule pair, dynein arms (inner and outer), radial spokes, nexin links, and the ciliary membrane. These structural elements are crucial for generating the rhythmic beating motion essential for mucociliary clearance. Defects in any of these components are directly implicated in the pathophysiology of Kartagener's Syndrome, resulting in impaired ciliary motility and associated clinical manifestations.

Symptoms

As a result, this condition produces prominent symptoms. Generally, the severity of symptoms differs from one individual to another. Polysplenia, complicated cardiac disease, and biliary atresia are common connections (6). Asthenozoospermia (lower or no sperm mobility) is the cause of infertility in men. Another possibility is that the epididymal duct's malfunctioning cilia are to blame (7). Ectopic pregnancies in women may occur because the egg does not reach the fertilization site and is implanted outside the uterus(8).

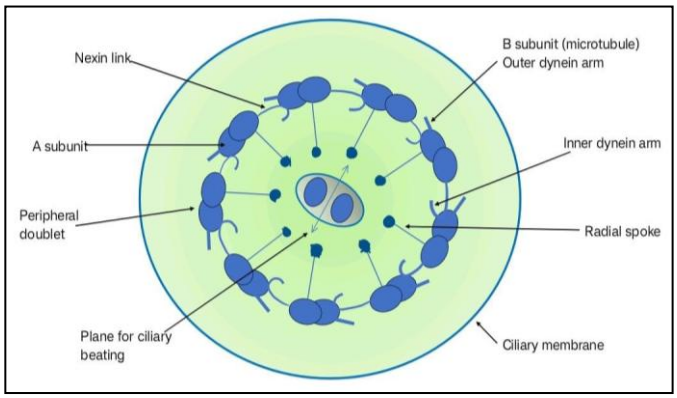

Fig. 3. The ultrastructure of motile cilia

This syndrome's first symptoms appear in the newborn stage. The disease can cause respiratory distress, coughing, choking, and gagging in newborns soon after birth (9). Since cilia are needed to remove amniotic fluid from the womb, if it is present, from a newborn's lungs, these occurrences are primarily caused by incorrect cilia movement (9). Because of the non-specific symptoms and the low level of disease awareness in primary care settings, the diagnosis frequently goes unrecognized. Moreover, more than one test is sufficiently accurate on its own to provide a conclusive diagnosis. Diagnosis is only available at highly specialized centres as these tests necessitate expensive, advanced equipment and expertise for precise processing and understanding. In countries with limited resources, the challenge is amplified due to the lack of expensive equipment and technical expertise (10). The purpose of this review was to clarify the need for a multidisciplinary strategy in the management of Kartagener's Syndrome.

Clinical Investigations

There are currently no international rules for performing and reporting testing, nor is there a globally accepted procedure that defines the diagnostic criteria. The majority of specialized facilities use "local" diagnostic algorithms (10). According to a European consensus declaration, a phenotype consistent with PCD should be seen, and diagnostic testing carried out at specialized centres should validate the diagnosis (4). Even though the literature currently in publication contains contradictory evidence, some structural changes that can be seen on paranasal sinus CT scans have been suggested as possible contributing causes to the development of chronic rhinosinusitis (CRS). It is important to note that structural variations such as fronto-ethmoidal cells, infraorbital ethmoid (Haller) cells, Concha Bullosa (CB), and Paradoxical Middle Turbinate (PMT) hinder adequate drainage from the frontal sinus or the ostiomeatal complex. (11).

Diagnosis

Since embryonic protein structures that direct organ development are shaped by genetic factors, abnormal ciliary function may have an impact on the location of internal organs.

Shaik Parveen, P. Sanjana, N. Sharanya, and D. Gowthami, "Ciliary Dysfunction: The Root Cause of Kartagener's Syndrome," *International Research Journal of Pharmacy and Medical Sciences (IRJPMS)*, Volume 8, Issue 2, pp. 52-55, 2025.

While some proteins, like Activin beta, are involved in right-sided development, others, such Sonic Hedgehog and Nodal play roles in development on the left side. Misplacements may result from disturbances in these procedures (15). Situs inversus totalis (complete organ reversal) or situs ambiguous (abnormal organ laterality)are common outcomes of conditions such as PCD (16). Divergent interpretations among experts, especially cardiologists, who link heterotaxy to certain cardiac abnormalities, add to this intricacy. About one in 10,000 people have heterotaxy, which involves different patterns of inheritance (17), (18). These anomalies in laterality and cardiac problems are caused by dysfunctional cilia in embryonic cells (16).

The non-specific signs of this disease, like persistent coughing and recurring respiratory infections, can make diagnosis difficult and cause delays (12). A comprehensive physical examination, medical history, and a series of tests are used to make the diagnosis because there is no gold standard test (12). In some areas, the social stigma associated with receiving a diagnosis of a hereditary condition or chronic sickness serves as a deterrent to people seeking medical care. The stigma's effect is exacerbated by the correlation between these illnesses and infertility (10). When combined with infertility worries, social stigma, especially surrounding chronic and genetic disorders, might prevent people from seeking medical attention. In addition to childhood complaints including repeated colds, ear discharge, and nasal congestion, patients usually appear with symptoms such as a cold, cough, difficulty breathing, expectoration, anosmia, and headaches (19), (20). Minority communities may have an underdiagnosis of this illness. Increased concentrations of inflammatory proteins like matrix metalloproteinases (MMPs) contribute to airway remodelling and inflammation in chronic respiratory disorders such as Secondary Ciliary Dyskinesia (SCD) and PCD which begin early and proceed in an unpredictable manner (21).

Treatment And Management

Although this syndrome has no known cure, so the primary aims of treatment are to keep airways clean and make it easier to remove debris, mucus, and thick, extra fluid. Airway clearance treatment is the name given to this therapeutic strategy (22). The lack of sperm motility causes infertility in males with Kartagener Syndrome. Simultaneously, it develops in females as a result of ovum transport impairment caused by the oviductal cilia's dyskinetic motion. Even with treatment, these patients typically have a bad prognosis. The patient may have a higher chance of developing tuberculosis in certain situations. Lower lobe bronchiectasis is often complicated by tuberculosis. Antibiotic control should be the main focus of treatment for recurring infections. Even while some data indicate that sinus surgery may be a good alternative for these TB patients, more research is still needed in this area (23).

Non-Surgical

Preventing respiratory infections is the main goal of medical management for a person with Kartagener Syndrome (19). To guarantee effective airway clearance, a number of techniques are used, comprising manual chest physical therapy, postural drainage, autogenic drainage, active cycle breathing, and physical exercise (24). Antibiotics, steroids, nebulization, and nasal decongestants are the main non-surgical therapy options. Supportive pulmonary treatment, antibiotics with sufficient pseudomonal coverage, and routine chest physical therapy are further conservative therapeutic strategies. Although it hasn't been thoroughly investigated in these patients, the benefits of DNase and other mucolytic medications like acetylcysteine and hypertonic saline may be investigated, particularly in those with persistent respiratory issues or recurring infections (25).

Surgical Treatment

Classifying malposition's and directing surgical procedures require an understanding of the exact layout of abdominal organs and the branching configuration of primary stem bronchi. While isolated laevocardia, situs ambiguous, and dextrocardia without situs inversus sometimes entail complex, numerous defects, dextrocardia accompanied by situs inversus usually shows the heart correctly positioned. About two out of every 10,000 babies have dextrocardia with full situs inversus, congenital cardiac disease is comparatively uncommon (about 3% of instances), and 20% of these patients may have Kartagener's syndrome. An estimated one in 50,000 births is the overall incidence (26), (27), (28), (29), and (30).

Lung transplant (26), laparoscopic sleeve gastrectomy in patients with Kartagener syndrome (27), and other examples are reviewed. Rhinolalia Clausa in a Kartagener Syndrome case (28). Kartagener's syndrome can be treated with endoscopic sinus surgery (29), and extracorporeal life support (30).

II. CONCLUSION

Kartagener's Syndrome is a rare autosomal recessive disorder characterized by three main symptoms: situs inversus, chronic sinusitis, and bronchiectasis. It stems from irregularities in the structure or function of cilia, which hampers mucociliary clearance and makes individuals more susceptible to respiratory infections. For effective management, it is essential to make a timely diagnosis through clinical evaluation, imaging, and genetic testing. The focus of treatment is on managing symptoms, which may involve antibiotics, airway clearance techniques, and surgery if needed. Kartagener's Syndrome, although uncommon, provides important insights into ciliary function and its effects on respiratory health. Further studies are necessary for the development of therapeutic interventions and enhancement of patient outcomes. To provide comprehensive care, a multidisciplinary approach is necessary. To improve the quality of life for those impacted, it is essential to raise awareness and facilitate early diagnosis.

REFERENCES

1. Mishra M, Kumar N, Jaiswal A, Verma A, Kant S. Kartagener's syndrome: A case series. Lung India. 2012;29(4):366.
2. Gupta S, Handa KK, Kasliwal RR, Bajpai P. A case of Kartagener's syndrome: Importance of early diagnosis and treatment. Indian J Hum Genet. 2012;18(2):263-7.
3. Skeik N, Jabr FI. Kartagener syndrome. Int J Gen Med. 2011;4:41-3. doi:10.2147/IJGM.S16181.
4. Olm MAK, Caldini EG, Mauad T. Diagnosis of primary ciliary dyskinesia. J Bras Pneumol. 2015;41(3):251-63.

Shaik Parveen, P. Sanjana, N. Sharanya, and D. Gowthami, "Ciliary Dysfunction: The Root Cause of Kartagener's Syndrome," *International Research Journal of Pharmacy and Medical Sciences (IRJPMS)*, Volume 8, Issue 2, pp. 52-55, 2025.

5. Ul Hassan A, Hassan G, Khan SH, Rasool Z, Abida A. Ciliopathy with special emphasis on Kartageners Syndrome. Int J Health Sci (Qassim). 2009;3(1):65-9.
6. Mathur P, Gupta R, Soni V, Ahmed R, Goyal RB. Biliary atresia associated with polysplenia syndrome, dextrocardia, situs inversus totalis and malrotation of intestines. J Neonatal Surg. 2014;3(1):9.
7. Sironen A, Shoemark A, Patel M, Loebinger MR, Mitchison HM. Sperm defects in primary ciliary dyskinesia and related causes of male infertility. Cell Mol Life Sci. 2020;77(11):2029-48.
8. Mummert T, Gnugnoli DM. Ectopic Pregnancy. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [cited 2024 Feb 17]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK539860/.
9. Reuter S, Moser C, Baack M. Respiratory distress in the newborn. Pediatr Rev. 2014;35(10):417-29.
10. Rumman R, Jackson C, Collins S, Goggin P, Coles J. Diagnosis of primary ciliary dyskinesia: Potential options for resource-limited countries. Eur Respir Rev. 2017;26(143):160058. [cited 2023 Nov 9]. Available from: https://err.ersjournals.com/content/26/143/160058.
11. Plantier DB, Pilan RRM, Athanazio R, Olm MAK, Gebrim EMS, Voegels RL. Computed tomography evaluation of the paranasal sinuses in adults with primary ciliary dyskinesia. Int Arch Otorhinolaryngol. 2023;27(1):e130-7.
12. Kugner M. Kartagener Syndrome Symptoms and Treatment. Verywell Health [Internet]. [cited 2023 Aug 19]. Available from: https://www.verywellhealth.com/kartagener-syndrome-2860366.
13. RESERVED IUAR. Orphanet: Primary ciliary dyskinesia [Internet]. [cited 2023 Jun 15]. Available from: https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=GB&Expert=244.
14. Zariwala MA, Knowles MR, Leigh MW. Primary Ciliary Dyskinesia. In: Adam MP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE, Bean LJ, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993 [cited 2023 Nov 9]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK1122/.
15. Reidy J, Sischy S, Barrow V. Anaesthesia for Kartagener's syndrome. Br J Anaesth. 2000;85(6):919-21. [cited 2023 Nov 9]. Available from: https://academic.oup.com/bja/article/85/6/919/250759.
16. Shapiro AJ, Davis SD, Ferkol T, Dell SD, Rosenfeld M, Olivier KN, et al. Laterality defects other than situs inversus totalis in primary ciliary dyskinesia. Chest. 2014;146(5):1176-86.
17. Richards AA, Garg V. Genetics of congenital heart disease. Curr Cardiol Rev. 2010;6(2):91-7.
18. Ware SM, Peng J, Zhu L, Fernbach S, Colicos S, Casey B, et al. Identification and functional analysis of ZIC3 mutations in heterotaxy and related congenital heart defects. Am J Hum Genet. 2004;74(1):93-105.
19. Kuehni CE, Lucas JS. Toward an earlier diagnosis of primary ciliary dyskinesia. Which patients should undergo detailed diagnostic testing? Ann Am Thorac Soc. 2016;13(8):1239-43.
20. Dell SD. Primary ciliary dyskinesia: Myths and realities. Paediatr Child Health. 2008;13(8):668-70.
21. Pifferi M, Bush A, Caramella D, Metelli MR, Di Cicco M, Piras M, et al. Matrix metalloproteinases and airway remodeling and function in primary ciliary dyskinesia. Respir Med. 2017;124:49-56. doi:10.1016/j.rmed.2017.02.001.
22. Belli S, Prince I, Savio G, Paracchini E, Cattaneo D, Bianchi M, et al. Airway clearance techniques: The right choice for the right patient. Front Med (Lausanne). 2021;8:544826. doi:10.3389/fmed.2021.544826.
23. Alduihi FA. Delayed diagnosis of Kartagener syndrome in a fertile young man-An unusual case. Eur Respir Pulm Dis [Internet]. 2019;(1):25-7. [cited 2023 Aug 16]. Available from: https://www.touchrespiratory.com/respiratory-infections/journal-articles/delayed-diagnosis-of-kartagener-syndrome-in-a-fertile-young-man-an-unusual-case/.
24. Mirra V, Werner C, Santamaria F. Primary ciliary dyskinesia: An update on clinical aspects, genetics, diagnosis, and future treatment strategies. Front Pediatr. 2017;5:135. doi:10.3389/fped.2017.00135.
25. Butt SRR, Shakoor H, Khan TJ, Almaalouli B, Ekhator C, Ansari S, et al. A rare case of Kartagener syndrome presenting with sinusitis, situs inversus, and bronchiectasis: Emphasizing early diagnosis and management strategies. Cureus. 2023;15(7):e41890.
26. Yamamoto H, Sugimoto S, Miyoshi K, Otani S, Yamane M, Toyooka S. Lung transplantation for Kartagener syndrome: Technical aspects and morphological adaptation of the transplanted lungs. Gen Thorac Cardiovasc Surg. 2021;69(3):588-92.
27. Burvill A, Blackham R, Hamdorf J. Laparoscopic sleeve gastrectomy in a patient with situs inversus totalis and Kartagener syndrome: An unusual surgical conundrum. BMJ Case Rep. 2019;12(7):e229550.
28. Raoufi M, Sator H, Lahma J, El Ayoubi A, Nitassi S, Oujilal A, et al. A case of Kartagener syndrome with rhinolalia clausa. Pan Afr Med J. 2016;23:159. doi:10.11604/pamj.2016.23.159.8664.
29. Tang X, Zou J, Liu S. Endoscopic sinus surgery for treatment of Kartagener syndrome: A case report. Balkan Med J. 2013;30(2):244-7.
30. Kundu R, Singh A, Datta P, Shrivastava A, Srinivasan S. Extracorporeal life support as rescue therapy in severe bronchiectasis with Kartagener's syndrome. Anaesthesiol Intensive Ther. 2022;54(4):334-8.