

CHAPTER VII

CONCLUSION

This cohort study is the first study in Indonesia using cytogenetic results and we can conclude:

1. Based on the cytogenetic results, we demonstrated that (69.6%) of patients had Female karyotype 46,XX, (22.8%) had chromosomal abnormality and (7.6%) had male karyotype 46,XY.
2. Based on the clinical profile of the patients 37,5% of patients had normal secondary sexual development Tanner stage (5). Majority of patients (87.5%) had normal female external genitalia Prader stage (0).
3. The most common causes of primary amenorrhea were gonadal dysgenesis due to Turner syndrome including its variants (21.25%), followed by MRKH by (17.5%) pure gonadal dysgenesis (6.3%), CAH (3.7%), CAIS (2.5%) and PAIS (1.26%).
4. The result of scoring system showed that patients with normal karyotype (46, XX or 46, XY) matched score 1 and 2 , while patients with chromosomal abnormalities (17/18) matched score 3 and 4.

Future direction

1. Further study with additional data includes hormonal tests, molecular analysis for further understanding of the characteristic of those patients and demonstrate the other causes of primary amenorrhea.
2. High number of patients with MRKH needs a molecular study to detect the gene mutation that can be associated.

3. Scoring system needs more study to distinguish whether it can be used as a clinical tool.

REFERENCES

1. Anagani M, Rathika A, Prabha B. Primary Amenorrhea - A One Year Review. *Obstetric and Gynecology journal* 2017;6(1):2–5.
2. Merin T, Rema D, Preetha T, Amudha S, Jayalakshamma J, Mary M. Amenorrhea : Cytogenetic Studies and Beyond. *American Journal of Molecular and Cellular Biology* 2012; 1: 25-37.
3. Malla TM, Dar FA, Pandith AA, Zargar MH. Frequency and pattern of cytogenetic alterations in primary amenorrhea patients of Kashmir , *North India. Egypt J Med Hum Genet.* 2016;17(1):25–31.
4. Butnariu L, Covic M, Ivanov I, Bujoran C, Gramescu M, Gorduză EV. Clinical and cytogenetic correlation in primary and secondary amenorrhea : retrospective study on 531 patients. *Revista Română de Medicină de Laborator*, 2011;19(2):51–60.
5. Prapa T, Trizae R. Current evaluation of amenorrhea. *Journal of sterility and fertility*; 2008;90(5):21–25.
6. Vijayalakshmi J, Koshy T, Kaur H, Mary FA, Selvi R, Parvathi VD, et al. Cytogenetic Analysis of Patients with Primary Amenorrhea. *Int J Hum Genet* 2010;10(3):71-76
7. Report C, Jahan S, Shermin S, Habib SH, Nayer R. Gynecology & Obstetrics Kallmann ' s Syndrome : A Rare Cause of Primary Amenorrhoea. *Journal Gynecol Obstet*; 2014;4(9).
8. Klein D, Poth M. Amenorrhea: An Approach to Diagnosis and Management. *Am Fam Physician.* 2013;87(11):781-788.
9. Leelavathy Nanjappa, Sayee Rajangam et al. Genotype – Phenotype Correlation in 46 , XY Females. *Kuwait Medical Journal*; 2008;40 (3): 225-229.
10. Hasan A, Hakan T, M. Hamza M. A New Female Patient with 47 , XXY Karyotype and SRY. *Andrology-Open Access*; 2016;5(1):10–13.
11. Chandrayan P, Parekh U, Jain N, Chandrayan P. Mullerian duct anomalies presenting with primary amenorrhoea. *Journal of Medicine*; 2016;5(2).
12. Pokale Y, Jadhav A, Kalthe B, Kate U. A patient of primary amenorrhea with 46 , XY Karyotype : Androgen insensitivity syndrome (AIS). *Journal Gyn and End.* 2013;5(5).
13. Okafor et al. Imperforate Hymen Presenting with Massive Hematometra and Hematocolpos : A Patient Report., *American Society for Reproductive Medicine*; 2015;5(10).

14. Allahbadia G, Human F. An Update on the Causes of Primary and Secondary Amenorrhea along with Aetiopathogenesis and Therapeutic Management Monograph Series. *avid Sci Monogr Ser.* 2016;9(6)
15. Afshar H, Najafipour R, Ansari J, Karimi N, Jalilvand M. cytogenetic analysis in woemen with primary and secondary amenorrhea R. *J Fundam Appl sceince. J Fundam Appl Sci.* 2016; 8(2S), 1173-1187.
16. Kim KS, Kim J. Disorders of Sex Development. *Korean Journal of Urology.* 2012;53(1):1-8.
17. Parikh RM, Nakum K, Kadikar GK, Gokhle A V. Mullerian anomalies : a cause of primary amenorrhea. *International Journal of Reprodction, Contraception, Obstet Gynecology.* 2013;2(3):3–7.
18. Mamoojee Y, Jones P, Stewart J, Choudhary M, Quinton R. Spontaneous resolution of secondary amenorrhoea in a patient with mosaic Turner ' s Syndrome. *Journal clinical genetics;* 2016;3(2);52-59.
19. Erinoloa A, Umila CL, Craiova F. Female reproductive tract misdevelopment : Comments on Mayer Rokitanski Küster Hauser syndrome. *Acta Endocrinologica (Buc.);* 2017;6(2);126-129.
20. Homa L, Thomas S, Sanfilippo J. Primary amenorrhea with transverse vaginal septum and scant hematocolpos : A patient report. *Avid Science Monograph Series;* 2012;2, 87-91.
21. Leigh B, Dorn C, Ulrich U. Gonadal dysgenesis. *Thesis;* 2009: 1-46.
22. Morgan T. Turner Syndrome: Diagnosis and Management. American Family Physician Web site at www.aafp.org/afp.2007.
23. Bharath R, Unnikrishnan AG, Thampy M V, Anilkumar A, Nisha B, Praveen VP, et al. Turner Syndrome and its Variants. *Indian Journal of human genetics;* 2010;77:2008–10.
24. Çatlı G, Alparslan C, Can Ş, Akbay S, Kelekçi S, Atik T, et al. Patient Report Gonadal Dysgenesis : Spontaneous Breast Development and Menstruation. *journal rare disorders;* 2015;7(2):159–62.
25. Cox L, Liu JH. Primary ovarian insufficiency : an update. *international Journal of Women Health;* 2014;235–43.
26. Meghan B, Oakes M, Aimee D. Complete androgen insensitivity syndrome associated with leiomyoma: patient report. *J Adolesc Gynecol.* 2015;3252.

27. Oakes MB, Eyvazzadeh AD, Quint E, Smith YR. Mini-Reviews Complete Androgen Insensitivity Syndrome — A Review. *J andrology* ; 2008;21 (6):5–10.
28. Motos M, Mendoza N. Androgen insensitivity syndrome Androgen insensitivity syndrome. *Journals Endocrinology*; 2014; 1(2), 20-25.
29. Kapoor K, Sarkar M Das, Pal DK. Partial Androgen Insensitivity Syndrome : A rare disease. *indian journal of Endocrinology and metabolism*; 2016;4(11):815–8.
30. Fourman L, Fazeli P. Neuroendocrine Causes of Amenorrhea — An Update. *Avid Science Monograph Series*, 2015;100(3):812–24.
31. Laitinen E. Kallman syndrome clinical and molecular genetic features *Thesis*, 2012.
32. Chiavaroli V, Adamo ED, Diesse L, Giorgis T De, Chiarelli F, Mohn A. Primary and Secondary Amenorrhea. *Journals of Human Genetics*; 2010;89(5):217-9.
33. Dover R. Primary & Secondary amenorrhoea overview. *Journal Reproduction and Health*; 2016;345(4):312-61.
34. Kelberman D, Rizzoti K, Lovell S, Robinson I, Dattani M. Genetic Regulation of Pituitary Gland Development in Human and Mouse. *Journals Genetics*;2009;790–829.
35. Doopadapalli D, Ray A, Lingegowda K. Patient Report Non-classical congenital adrenal hyperplasia presenting as primary amenorrhoea with virilization. *Clin Exp Reprod Med*;2015;4(5): 29–32.
36. Kelberman D, Rizzoti K, Lovell-badge R, Robinson ICAF, Dattani MT, Kelberman D, et al. Genetic Regulation of Pituitary Gland Development in Human and Mouse. *Acta Endocrinol*; 2009;790–829.
37. Cs B, Doopadapalli D, Ray A, Lingegowda K. Patient Report Non-classical congenital adrenal hyperplasia presenting as primary amenorrhoea with virilization. *Arac Rec*;2015;4(5):1627–9.
38. Gürsoy S, Kılıçarslan ÖA, Bozkaya ÖG, Bora E, Ünal N, Erçal D. Clinical and Cytogenetic Evaluations of Patients with Turner Syndrome : Are We Aware Enough ? *Italian Study Group for Turner's Syndrome. J Clin Endocrinol Metab*; 2017;39(November 2015):2015–8.
39. Mohamad K, Jamshidi L, Jelyani KN. Is Age of Menarche Related with Body Mass Index ? *Acta Endocrinol*;2013;42(9):1043–8.
40. Master-hunter T, Medical M, Arbor A. Amenorrhea : Evaluation and Treatment. *Int J Hum Genet,s*;2006; 4 (2): 25-30.

41. Bettiayah R, Daksha S, Ghanti R, Balakrishnan D. Patient Report Female genital tuberculosis – still a common cause of primary amenorrhea in developing countries.; *Gynecol Obstet (Sunnyvale)* 16;5(8):2891–4.
42. Utiirrez RLVAO. prevalence of chromosomal aberration in Mexican women with primary amenorrhea. *Clin Endocrinal Metab* ;2007;15(4).
43. Marzuki NS, Anggaratri HW, Suciati LP, Ambarwati DD, Paramayuda C, Kartapradja H, et al. Diversity of sex chromosome abnormalities in a cohort of 95 Indonesian patients with monosomy X. *Mol Cytogenet*; 2011;4(1):23.
44. Kwon S, Chae H, Lee K, Kim S, Kim C, Kang B. Causes of amenorrhea in Korea : Experience of a single large center. *Journals clinical genetics*; 2014;41(1):29–32.
45. William, D. Prader Staging. *Best Pract Res Clin Endocrinol Metab*. 2010;24(2):163–86.
46. Williams textbook of *Endocrinology*, 12th Ed, Chapter 23, Page 881.
47. Tanner staging. 2017; Retrieved from: *emedicine.medscape.com*.
48. www.wikipedia.org/wiki/List_of_average_human_height_worldwide
49. Soliman A, De Sanctis V, Elalaily R. Nutrition and pubertal development. *Indian Journal of Endocrinology and Metabolism*. 2014;18(1):39-47.