Genetic Abnormalities of Primary Amenorrhea in Women from the South of Iraq

Saad A. Al Omar [1], Zinah Anas Salman [2], Ahmed Kamal Kasim [3]

1. Department of Pathology, College of Medicine, University of Basrah, Basrah, Iraq.
2. Department of Pediatrics, Maternity and Pediatric General Hospital, Basrah Health Directorate.
3. Department of Cytogenetics, Baghdad Teaching Laboratories, Medical City, Baghdad.

Received: 2.1.2024 **Accepted: 16.1.2024**

Abstract:

Background: Genes and hormones play an important and complicated role in differentiating the gonads to the testis or ovary. Primary or secondary amenorrhea is either absence or unexpected early end of menstruation. Hormonal, physiological, environmental and genetic reasons are all involved in developing such a disorder. Diagnosis is very important to provide the required treatment and one of the powerful diagnostic goals is Karyotyping.

Aim of study: So, the study aimed to identify the chromosomal abnormalities through karyotyping and how frequent each is.

Methods: Samples of 174 patients who were referred to AlBayan Private Laboratory in Basrah City from 2018 to 2022

Results: A total of 174 patients were diagnosed with PA and the results showed that out of 174 patients, 57(30%) were diagnosed with chromosomal abnormalities using cytogenetics. Karyotype analysis showed that 46, XY represented more than 50% of the genetic abnormalities, followed by 27% and 3% due to 45, X or 46, X, i(Xq) respectively. However, all the rest abnormalities displayed the same percentage, 1% of the total number of PA patients. Our study showed that a significant number of cases with primary amenorrhoea harbor chromosomal abnormalities, which are significant in gonadal dysgenesis.

Conclusion: So genetic counselling, routine chromosomal study, hormonal assessment, and radiological evaluation are important for proper management, also the hormonal replacement for Turner Syndrome patients, and screening for malignancy in patients with sex reversal are important

Keywords: primary amenorrhea, karyotyping, chromosomal abnormalities, congenital anomalies

Corresponding author: Saad A. Al Omar

College of Medicine, University of Basrah, Basrah, Iraq.

✉ **E-mail:** saad.abdullah@uobasrah.edu.iq

Introduction

Normally, the menstrual function is expected at puberty, but if this doesn't happen then it is a disease called primary amenorrhea (PA) (1), which is defined as no pubertal signs, by the age of 13 years or 5 years after breast development and no menarche occurs. When the menstruation ceases after regular cycles this is called secondary amenorrhea (2). Karyotype analysis shows that 3.4% of PA patients are XY females. Despite that the incidence of PA doesn't exceed 5%, the incidence is increasing due to better registration, social media and better health care (3). One of the main reasons for PA is the congenital anomalies including Mullerian aplasia or Mayer-Rokitansky-Kuster Hauser Syndrome (MRKHS) (4). This involves the absence of the uterus and vagina in addition to obstruction of the reproductive tract. Gonadal dysgenesis could be considered as another reason for PA (5). Hypothalamic disorders are also counted as one of the main reasons which could be represented as a gonadal or/and ovarian disorder (6). One of the diagnostic keys of PA is karyotyping to identify the genetic abnormalities underlying this disorder with various percentages of each chromosomal defect (7). So, the study aimed to identify the chromosomal abnormalities, how frequent each is in patients and the value of knowing the genetic reason to treat accordingly.

10.33762/mjbu.2024.145705.1183

Materials & methods

The present work is a descriptive study conducted at Albayan Private Diagnostic Laboratory from 2018 to 2022. The data were collected relying on the patient's medical history, records, and physical examination.

Methods

Two ml of peripheral blood was aspirated under an aseptic technique, collected in a heparin sodium tube, and cultured within 24 hours in lymphocyte culture media. The medium was prepared by RPMI 1640, 10% fetal bovine serum, L-Glutamine, HEPES buffer, penicillin/ Streptomycin, and Phytohemagglutinin, for 69 hours, at 37 C, 100 uL of colcimide added for metaphase arrest for 30 minutes, then we proceed for harvesting of the chromosomes, by doing hypotonic treatment with 0.75mol KCl, and 3 washes of freshly prepared chilled fixative, then the slides were read using Trypsin-Giemsa- Trypsin Banding., and analysis using 540 resolution (8).

Results

The results showed that out of 174 patients, 57 (30%) were diagnosed with chromosomal abnormalities using the cytogenetics approach Figure 1. The karyotype analysis showed that 46, XY represented more than 50% of the genetic abnormalities, followed by 27% or 3% due to 45, X or 46, X,i(Xq) respectively. However, all the rest abnormalities displayed the same percentage, 1% of the total number of PA patients A= non-turner = mos45X46XY, Terner =, mos45X,46XX mos45X,46X, (isoXq)isox Figures 2 & 3.

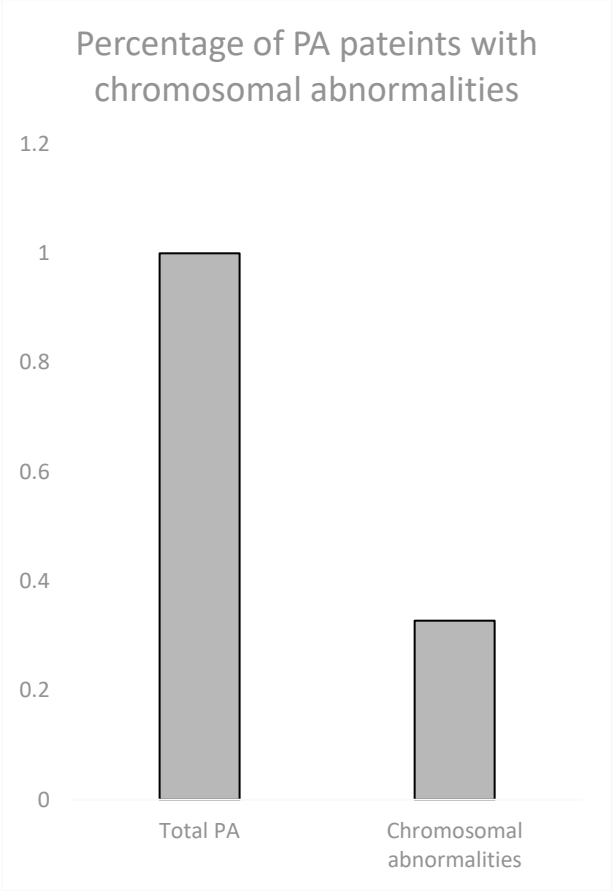

Figure 1: Percentage of PA patients with chromosomal abnormalities (total)

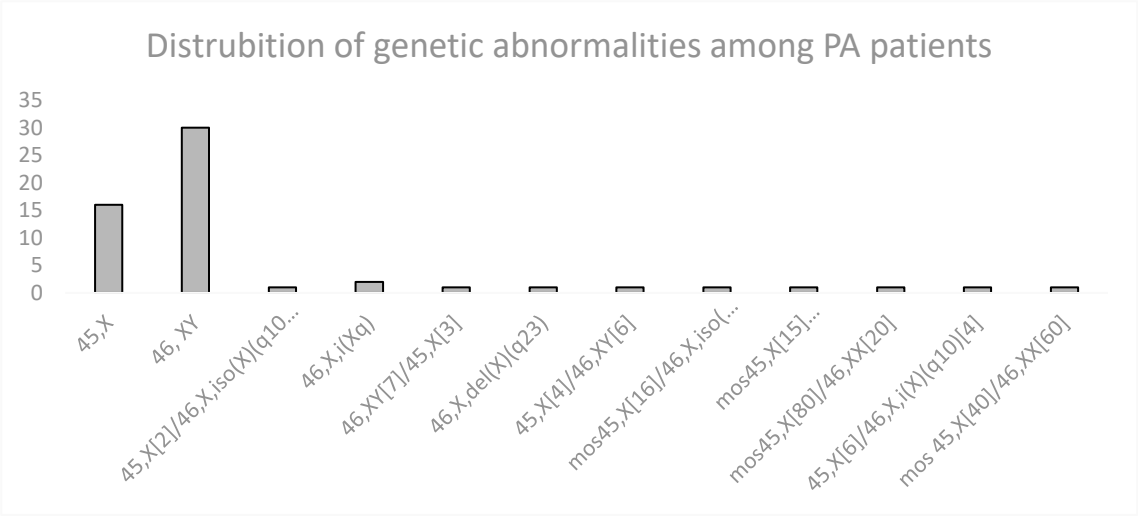

Figure 2: Percentage of Distribution of genetic abnormalities among PA patients

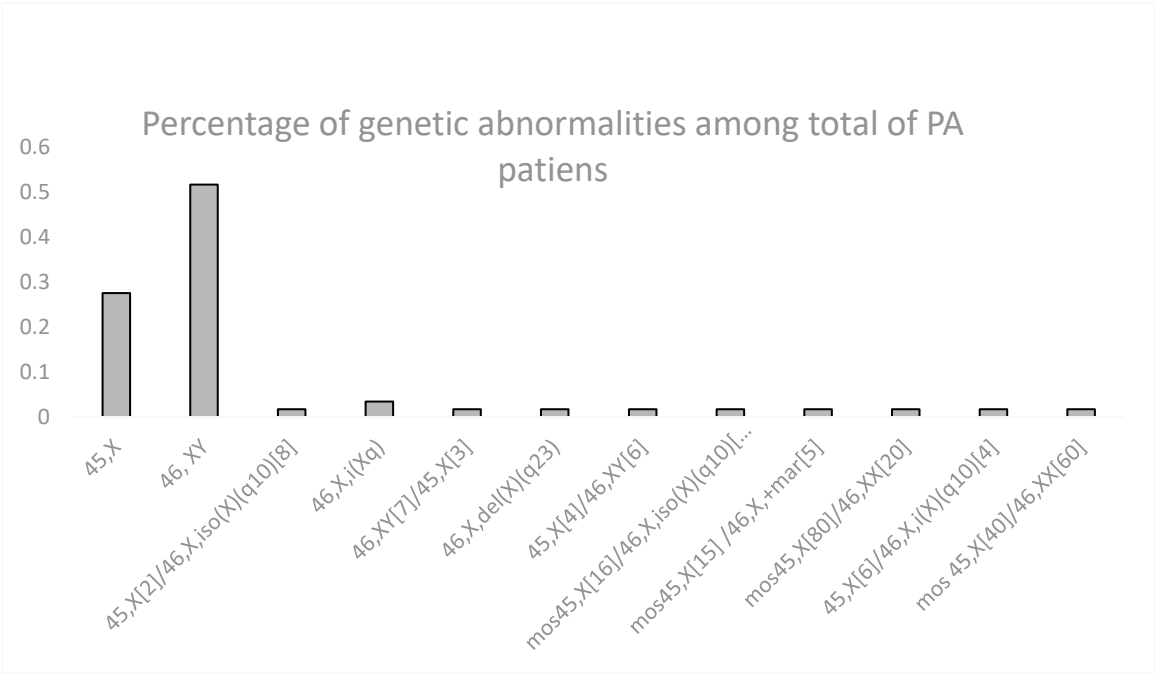

Figure 3: percentage of genetic abnormalities among PA patient

Discussion

Genetic and endocrine abnormalities mainly are the two reasons for PA with different genetic abnormalities. The results showed that the incidence

of genetic abnormalities was about 33%. Cytogenetic analysis of the referred PA patients is very critical due to its importance in particular for SA patients in reproduction and genetic counseling. This percentage is 10% higher than (9,10). Furthermore, the results are two-fold higher than (11). However, the results come in agreement with (12) who reported chromosomal abnormalities in 34% of the PA patients. The relatively high percentage of genetic defects might be attributed to the polluted areas and lands of Iraq especially in the south with chemicals, herbicides, and heavy metals. Other factors could be implicated such as the nutrition and the mother's age and health reviewed by (13).

Obviously, the 46, XY set was the highest abnormality among the total genetic disorders reaching more or less 50%. This defect could be explained by the possibility of high gene frequency of androgen insensitivity in the community of Sout of Iraq, which needs further evaluation.

Conclusion:

Our study showed that a significant number of cases with primary amenorrhea harbor chromosomal abnormalities, which are significant in gonadal dysgenesis. So genetic counselling, routine chromosomal study, hormonal assessment, and radiological evaluation are important for proper management, also the hormonal replacement for Turner Syndrome patients, and screening for malignancy in patients with sex reversal are important.

References

1- Federman, D.D. (1979). Primary Amenorrhoea. The West. J. Med.

(Klein & Merrily, 2013) Amenorrhea: An Approach to Diagnosis and Management.

2- Klein DA, Poth MA. Amenorrhea: an approach to diagnosis and management. Am Fam Physician. 2013 Jun 1;87(11):781-8. PMID: 23939500.

3- Wachtel, S. S. (1979). The genetics of intersexuality: clinical and the oretic perspectives. *Obstetrics and Gynecology*, *54*(6), 671-685.

4- Grimbizis GF, Gordts S, Di Spiezio Sardo A, Brucker S, De Angelis C, Gergolet M, Li TC, Tanos V, Brölmann H, Gianaroli L, Campo R. The ESHRE/ESGE consensus on the classification of female genital tract congenital anomalies. Hum Reprod. 2013 Aug;28(8):2032-44. doi: 10.1093/humrep/det098. Epub 2013 Jun 14. PMID: 23771171; PMCID: PMC3712660. https://doi.org/10.1093/humrep/det098

5- Mannaerts D, Muys J, Blaumeiser B, Jacquemyn Y. A rare cause of primary amenorrhoea, the XY female with gonadal dysgenesis. BMJ Case Rep. 2015 Feb 9;2015:bcr2014206609. https://doi.org/10.1136/bcr-2014-206609

6- Schorge, J.O. & Schaffer, J.I (Eds.), Williams gynecology, McGraw Hill, New York, NY (2008), pp. 1112-1128

7- Zhao X, Shen GM, Feng Q, Sun XG, Luo Y. [Cytogenetic studies of 131 patients with primary amenorrhea (including three novel abnormal karyotypes)]. Yi Chuan. 2008 Aug;30(8):996-1002. Chinese. doi: 10.3724/sp.j.1005.2008.00996. PMID: 18779148.
https://doi.org/10.3724/sp.j.1005.2008.00996

8-Rooney, D. E. (Denise E.) (2001). Human cytogenetics: constitutional analysis; a practical approach. Oxford: Oxford University Press.

9- Rajangam S, Nanjappa L. Cytogenetic studies in amenorrhea. Saudi Med J. 2007 Feb;28(2):187-92. PMID: 17268694.

10- Dutta UR, Ponnala R, Pidugu VK, Dalal AB. Chromosomal abnormalities in amenorrhea: a retrospective study and review of 637 patients in South India. Arch Iran Med. 2013 May;16(5):267-70. PMID: 23641739.

11- Demirhan O, Tanrıverdi N, Tunç E, Inandıklıoğlu N, Süleymanova D. Frequency and types of chromosomal abnormalities in Turkish women with amenorrhea. J Pediatr Adolesc Gynecol. 2014 Oct;27(5):274-7. doi: 10.1016/j.jpag.2013.11.013. Epub 2014 Jul 9. PMID: 25023981. https://doi.org/10.1016/j.jpag.2013.11.013

12- Samarakoon L, Sirisena ND, Wettasinghe KT, Kariyawasam KW, Jayasekara RW, Dissanayake VH. Prevalence of chromosomal abnormalities in Sri Lankan women with primary amenorrhea. J Obstet Gynaecol Res. 2013 May;39(5):991-7. doi: 10.1111/j.1447-0756.2012.02063.x. Epub 2012 Dec 21. PMID: 23279116. https://doi.org/10.1111/j.1447-0756.2012.02063.x

13- Al-Hadithi, T.S., Al-Diwan, J.K., Saleh, A.M. *et al.* Birth defects in Iraq and the plausibility of environmental exposure: A review. *Confl Health* **6**,3 (2012). https://doi.org/10.1186/1752-1505-6-3.