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Maternal Age Distribution of Down-Syndrome at Pediatric Growth and Development Clinic, 2015-2019

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ABSTRAT

Introduction: Down Syndrome is a common chromosome abnormality among infants. This condition is Present in 1 over 800 deliveries. Advanced maternal age is a risk factor for Down syndrome. Other miscellaneous factors are radiation, infection, autoimmune and paternal age. The Aim is to determine maternal age distribution of Down syndrome at pediatric growth and development polyclinic, Wahidin Sudirohusodo hospital.

Methods: A Descriptive study. Study population was all outpatients at Pediatric Growth and Development polyclinic, Wahidin Sudirohusodo hospital in Makassar 2015-2019. Samples in this study were collected from total sampling of population data that met the criteria of new Down syndrome patients with complete medical records

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Results: This study found 237 new pediatric down syndrome patients admitted to growth and development polyclinic from January 2015 – December 2019, 95 complete medical records from 237. 52% (49) boys, 48 % (46) girls from 95 children. No gender difference was found in the presentation. Parental age of Down syndrome patients, the most advanced maternal age was >35, found 46 (48,42%), the most advanced paternal age was >35, found 63 (66,32%). Parity < 3rd, the most maternal age between 25-35 (23,16%), parity ≥ 3rd, the most maternal age was >34, found 30 (31,57%).

Conclusion. Advance maternal and/ or paternal age is a risk factor of Down Syndrome.

Keywords: Maternal age; Down Syndrome; Child growth and development

Introduction

Down Syndrome is a common chromosome abnormality among infants. This condition presents in 1 over 800 deliveries. Most of the cases (92.5%) due to nondisjunction; as a result of nondisjunction, fertilized ovum comprised from three duplication of chromosome 21 (trisomy 21); using standard cytogenetic nomenclature, trisomy 21 set as 47, XXX, +21 or 47, XY, +21. [1]

In 1866, John Langdon Haydon Down initially described clinical features and health problems corresponding with Down Syndrome. Lejune and Jacobs, in 1959, first time found this abnormality due to Trisomy 21. This trisomy consists of 3 types. First, nondisjunction or failure of separation during meiotic phase of the oocyte. This is the most common type (94%) in Down Syndrome. Second, a translocation type which consists of some or entire extra chromosome 21 joining with other chromosomes (chromosome 14, or 15, or 21, or 22), this type covers 3.5% of the cases. Third, a mosaic type. A mixture between normal diploid and cell that develops trisomy 21, nondisjunction occurs in mitosis during early embryogenesis; covers 2,5% of the cases.

First type related to the increasing maternal age during conception. On the second type, no age related found, around 75% translocation occurs de novo, and around 25% occurs genetically. The third type, mosaic, usually owns phenotype features slightly better than trisomy 21 or translocation of chromosome 21.[2]

Light/moderate cognitive disturbance is a characteristic of Down-Syndrome, such as hypotonic. This newborn could develop long-term physiology icterus, polycythemia and temporary leukemoid reactions. Eating disorders may develop during the infant period. Around one- third to half of Down syndrome child, frequently develop endocardial or other septal disorders. [3]

Advanced maternal age is a risk factor of down syndrome, but recent studies showed that young maternal age are vulnerable. [4] Many cases of child with down syndrome from young mothers were related with alcohol, cigars, poison and drugs that may cause nondisjunction. [5] Other miscellaneous factors are radiation, infection, autoimmune and paternal age. [2]

World Health Organization (WHO) 2018 estimates there are 8 million with syndromes disability in the

world. Specifically, there are 3,000-5,000 children born with chromosomal abnormalities per year. Riset Kesehatan Dasar (Riskesdas) 2018, Health ministry has announced, in Indonesia, there were 0.12% people with Down syndrome in 2010. This figure increased to 0.13% in 2013 and in 2018 increased to 0.21%. The number of new cases of Down syndrome outpatients in Indonesia hospital based from SIRS Online report 2015 data found 768 men, 889 women, in 2016 2,238 men, 2,011 women, and 2017 2,006 men, 2,124 women. [6,7,8]

This study aims to determine maternal age distribution of Down syndrome at Pediatric Growth and Development Polyclinic, Dr. Wahidin Sudirohusodo hospital in Makassar for the period of 2015-2019.

Methods

This study is a retrospective method with data collection of Down syndrome outpatient medical records at Pediatric Growth and Development, Wahidin Sudirohusodo hospital for the period of 2015-2019.

The study population was medical record data of outpatients at Pediatric Growth and Development, Wahidin Sudirohusodo from January 2015 to December 2019. Samples in this study were collected from total sampling of population data that met the criteria of new Down syndrome patients with complete medical records.

Result

In this study, 237 children admitted to Growth and Development clinics as new Down syndrome patients from January 2015 to December 2019, 95 were obtained from 237 complete medical record data. Table 1 shows the characteristics of Down syndrome patients, male 49 (51.57%) and female 46 (48.43%). Observed from the age of visitation at Growth and Development clinic, Wahidin Hospital, the most cases are between 1 month - 2 years of age, counted as 74 children (77.89). The order of delivery in most Down syndrome patients found the third parity 30 (31.57%) and the first parity 28 (29.47%). Planned pregnancies were 65 (68.42%) and the unplanned were 30 (31.52%).

Table 1. Characteristics of Down Syndrome Patients

Characteristics	n	%
Gender		
Male	49	51,57
Female	46	48,43
Age of visitation		
1 month - 2 years	74	77,89
3 years- 4 years	10	10,61
5 years-6 years	5	5,2
7 years-8 years	1	1,05
9 years-10 years	2	2,1
11 years-12 years	2	2,1
13 years-14 years	1	1,05

Parity		
1st	28	29,47
2nd	17	17,89
3rd	30	31,57
4th	13	13,71
5th	3	3,16
6th	2	2,1
7th	2	2,1
Planned/ Unplanned pregnancies		
Planned	65	68,42
Unplanned	30	31,52

Table 2 shows maternal age from children with Down syndrome, 46 (48.42%) >35 years old (48.42%), age between 35-35 years old 43(45.26%). Most paternal age > 35 years old were 63 (66.32%), age between 25-35 years were 29 (30.53%).

Table 2. Maternal and Paternal Age

Age (years)	Maternal		Paternal	
	n	%	n	%
<25	6	6,32	3	3,16
25-35	43	45,26	39	30,53
>35	46	48,42	63	66,32

Table 3 parity and maternal age, parity < 3rd the most maternal age between 25-35 years old were 22 (23,16%), parity ≥ 3rd the most maternal age >35 years old were 30.

Table 3. Parity and Maternal Age

Parity and Maternal age	n	%
< 3rd		
< 25 years	6	6,32
25 - 35 years	22	23,16
> 35 years	16	16,84
≥ 3rd		
< 25 years	0	0
25 - 35 years	21	22,11
> 35 years	30	31,57

Table 4 shows the hemoglobin levels of patients with Down syndrome when they first admitted at Pediatric Growth and Development Clinic, Wahidin hospital. The table shows the list of hemoglobin levels by age. At <6 months, 3 had hemoglobin levels below normal <9 g / dl. For ages between 6 months-6 years, 11 had hemoglobin levels below normal <11 g / dl. Between 6 years and 12 years of age, there are no hemoglobin levels below normal. The ferritin level of Down syndrome patients when first admitted at Pediatric Growth and Development Clinic, Wahidin hospital. The highest ferritin levels between 30-100, 28

(48.28%), the ferritin levels <30 were 22 (37.93%).

Table 4. Hemoglobin and ferritin level of patients with Down syndrome

Level	n	%
Hb		
< 6 month		
<9 gr/dl	3	9,09
>9 gr/dl	30	90,91
6 month – 6years		
<11 gr/dl	11	22,44
>11 gr/dl	38	77,56
>6 years		
<12 gr/dl	0	0
>12 gr/dl	7	100
Ferritin		
<30	22	37,93
30-100	28	48,28
>100	8	13,79

Table 5 shows the examination of FT4 and TSHS levels in Down syndrome patients when first admitted at Pediatric Growth and Development Clinic, Wahidin hospital. 81 showed normal FT4 levels and only 1 had low Ft4 levels. Normal children's TSHS level was 38, and those who experienced an increase of TSHS were 50.

Table 5. FT4 and TSHS level of patients with Down syndrome

	FT4			TSHS		
	<0,3	0,3-1,71	1,71	<0,27	0,27-4,2	>4,2
Total	1	81	6	0	38	50

Discussion

In this study, 237 children with Down syndrome enrolled at Pediatric Growth and Development Clinic from January 2015-December 2019, from 237 complete medical record data were obtained, namely 95 children. 95 male 49 (51.57%) and 46 female (48.43%) the prevalence of Down syndrome based on gender was not significant difference, this is in line with the results of new Down syndrome outpatients in Indonesia hospital based from SIRS Online report 2017 data for male 2,006, female 2,124.[6]

Down syndrome is categorized into three types based on its pathogenesis, failure to separate (nondisjunction), translocation, and mosaic. The category of nondisjunction Down syndrome related to maternal age. The age of the pregnant mother is related to the length of meiosis. The length of time allows the destruction of proteins that have a role in the process of separating chromosomes 7, in this study maternal age > 35 years was 48.42%. In line with previous studies, Down syndrome increases in maternal age over 30 years to 45 years. On the other hand, the age of the paternal has a minor role in the occurrence of Down syndrome. A recent systematic review study concluded that paternal age is associated with a slight increase in the

incidence of trisomy 21. Paternal age over 49 years showed an increased incidence of Down syndrome .[10] Age-related epigenetic changes in sperm. In men, age has an impact on mitosis rather than meiosis. Although mitotic errors are thought to be more relevant in older age, paternal meiotic errors are reported to account for about 10% of Down's syndrome cases.[11]

In this study, the percentage of young mothers with Down syndrome children was quite high. Research in Bosnia and Herzegovina shows the prevalence of young mothers with Down syndrome children were due to only advance maternal age were able to undergo amniocentesis and those who have large percentage of pregnancies with Down syndrome end in abortion. It is likely that young mothers lack sleep, an unbalanced diet, a lot of burden that leads to an unhealthy pregnancy. Habitual risk factors for young mothers and often associated with unwanted pregnancy.[5]

There have also been reports of a positive association between parity and Down syndrome in women who are younger (less than 35 years) and older (over 35 years). Women with parity> 3 should have prenatal screening for Down's syndrome. In this study, the frequency of Down's syndrome delivery is higher in the third child onwards, which is in line with previous studies. Therefore higher parity is a contributing factor in bearing a child with Down syndrome. [12]

The age of the mother and / or father is a risk factor for Down's syndrome, this study shows that young mothers are also vulnerable. A study in India found that 80.7% of trisomy 21 children were born to mothers aged 30 years, even though the mean age, 23 was low, 17 years was the first child.[13]

Hb levels that were below normal were only found in some patients, but ferritin levels were between 30-100, around 48.28 %%. This study shows that most children still experience iron depletion. The incidence of iron deficiency anemia in children with Down syndrome is increasing. Recommendations for anemia screening are based on the fact that irreversible cognitive impairment is associated with iron deficiency anemia and as children with Down syndrome are at higher risk for neurocognitive deficits. Previous research has shown lower iron intake among 10 children with Down syndrome. This is due to eating disorders in children with Down syndrome.[14]

Down syndrome is associated with an increased risk of endocrine disorders, especially thyroid disorders. The prevalence of congenital hypothyroidism in Down syndrome is estimated to be 28-35 times higher than the prevalence in the general population. Most of the reported cases of congenital hypothyroidism are due to thyroid hypoplasia. Normal FT4 levels were 81 children, but there were many increases in TSHS levels, namely 50 children. The presence of congenital hypothyroidism which is a differential diagnosis of Down syndrome. One of the other types of disorders is subclinical hypothyroidism, increased TSHS and normal thyroid hormone. In this study most likely were subclinical hypothyroidism. [15]

Conclusion

The advanced age of the mother is a risk factor for Down syndrome. Our results also show a high incidence of Down's syndrome in the maternal age group <35 years, and a reason for a multidisciplinary approach to identify triggers for trisomy.

Suggestion

Further study to assess risk factors and conditions during pregnancy can help us to develop strategies that minimize the incidence of Down syndrome.

References

1. Wayne H. Examination paediatrics 5th Edition A guide to paediatric training. Elsevier. 2019; 336-348
2. Soetjiningsih. Konsep Dasar Tumbuh Kembang Anak. In: Ranuh IGNG, penyunting. Tumbuh Kembang Anak. Edisi 2. Jakarta: EGC. 2017; 490-505.
3. William WH, Mayron JL, Robin RD, Mark JA, Current Diagnosis and treatment Pediatrics, 23nd edition (Lange). 2016; 1151.
4. Das H, Kusre G, Panyang R, Gogoi A, Shankarishan P, Nirmolia T. Study of the Relation of Maternal Age with Down Syndrome. International Journal of Health Information and Medical Research. 2(2): 9-12.
5. Sotonica M, Mackic-Djurovic M, Hasic S, Kiseljakovic E, Jadric R, Ibrulj S. Association of Parental Age and the Type of Down Syndrome on the Territory of Bosnia and Herzegovina. Med Arch. 2016; 70(2): 88-91.
6. Winurini S. Tantangan Pemerintah dalam mendukung penyandang Down Syndrome (DS) di Indonesia. Bidang Kesejahteraan Sosial, Info Singkat, Kajian Singkat Terhadap Isu Aktual dan Strategis. Jakarta: Pusat Penelitian Bidang Keahlian DPR RI. 2018; 10(6): 13-18.
7. Pusat data dan informasi kementerian kesehatan RI. Sindrom Down. 2018.
8. World Health Organization Regional Office for Europe (2018) Births with Down's syndrome per 100 000 live births. 2018. Available from: https://gateway.euro.who.int/en/indicators/hfa_603-7120-births-with-downs-syndrome-per-100-000-live-births/
9. Rayman R, Rahmanisa S, Putri GT, Hubungan Usia Ibu dengan Kejadian Sindrom Down. Medula. 2017; 7(5): 144-148.
10. Thompson JS. Disentangling the roles of maternal and paternal age on birth prevalence of Down syndrome and other chromosomal disorders using a Bayesian modeling approach. BMC Medical Research Methodology. 2019; 19:82. Available from: https://doi.org/10.1186/s12874-019-0720-1
11. Sharma R, Agarwal A, Rohra VK, Assidi M, Abu-Elmagd M, Turki RF. Effects of increased paternal age on sperm quality, reproductive outcome and associated epigenetic risks to offspring. Reprod Biol Endocrinol. 2015;13:35. doi: 10.1186/s12958-015-0028-x
12. Aldhwayan M, Al-Muammar MN, Alorf S, Am-Moajel A, El-Shafie M, Siddiqui AA, Khan F. Awareness among mothers of Down syndrome children on the importance of folic acid consumption during pregnancy. International Journal of Biomedical Research. 2015; 6(11): 903-908. DOI: https://doi.org/10.7439/ijbr.v6i11.2709 .
13. Jyothy A, Rao GN, Kumar KS, Rao VB, Devi BU,Reddy PP. Translocation Down Syndrome. Indian J Med Sci. 2002; 56(3):122-126.
14. Abdullah AD, Abdulali AA, Abdulaziz AN, Mohammed SA, Seraj AA, Khaled AS dkk. Anemia and Other Hematologic Disorder in Children with Down Syndrome. EC Microbology 2019; 15(12): 1-7.
15. Nermine HA. Thyroid disorders in subjects with Down syndrome: an update. Acta Biomed. 2018; 89(1): 132-139. doi: 10.23750/abm.v89i1.7120.