CHAPTER V

RESULTS

Seventy nine patients were included out of 98 patients of primary amenorrhea, the 19 patients were excluded because of unavailable data of one of the following data: weight, height, Tanner stage or Prader stage. The data was obtained from molecular and cytogenetic laboratory archive of Center for Biomedical Research, Faculty of Medicine Diponegoro University Semarang, from the period January 2004 until January 2017. The medical records of all patients whom referred with primary amenorrhea were reviewed including clinical evaluation and Karyotype results.

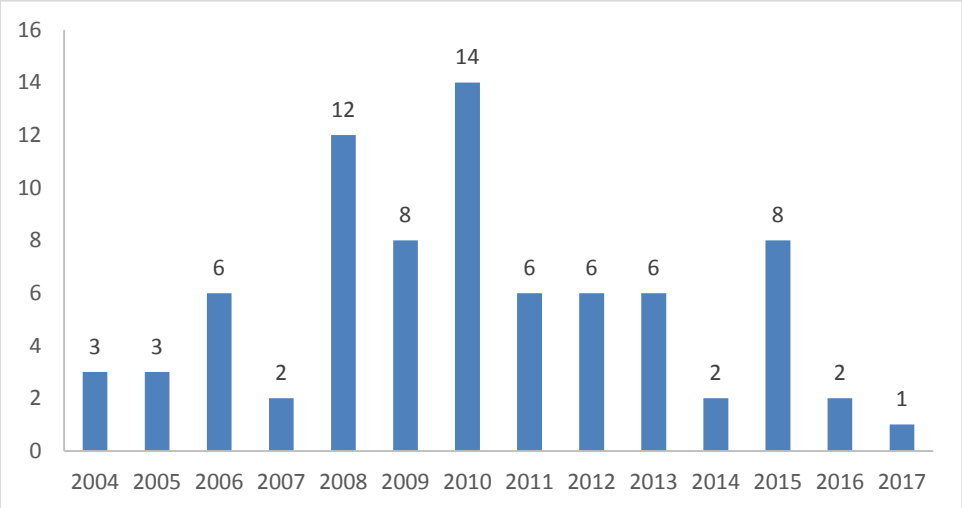

Figure 5. Distribution of primary amenorrhea patients per year (January 2004-january 2017)

The distribution of patients according to the karyotype results revealed that 55 (69.6%) of patients had 46, XX karyotype, six (7.6%) patients had 46, XY

karyotype and 18 (22.8%) patients with chromosomal abnormalities as showed in Figure 6.

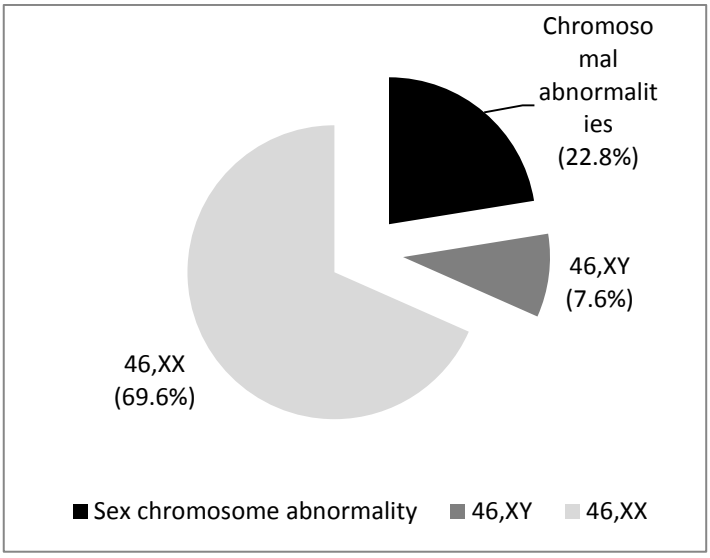

Figure 6. Distribution of karyotype results in primary amenorrhea patients

Karyotype results

In this study the Karyotype results of 79 patients revealed 55 (69.6%) patients with female karyotype 46, XX and six (7.6%) patients with male karyotype 46, XY. the most frequent chromosomal abnormality was monosomy X in 10.1% followed by mosaic cell line 45, X/46,XX by 3.7% . Isochromosome 45 X/46, X,iXq accounted 3.8%. Mosaicism with Y constitution 45,X/46,XY was seen in 2 patients 2.5%, marker chromosome 45,X/46,X +mar2% in one patient and chromosome 1 and X translocation 46,XX,t(1;X)(p34;q25) detected in one patient. The Karyotype results of all the patients showed in Table3.

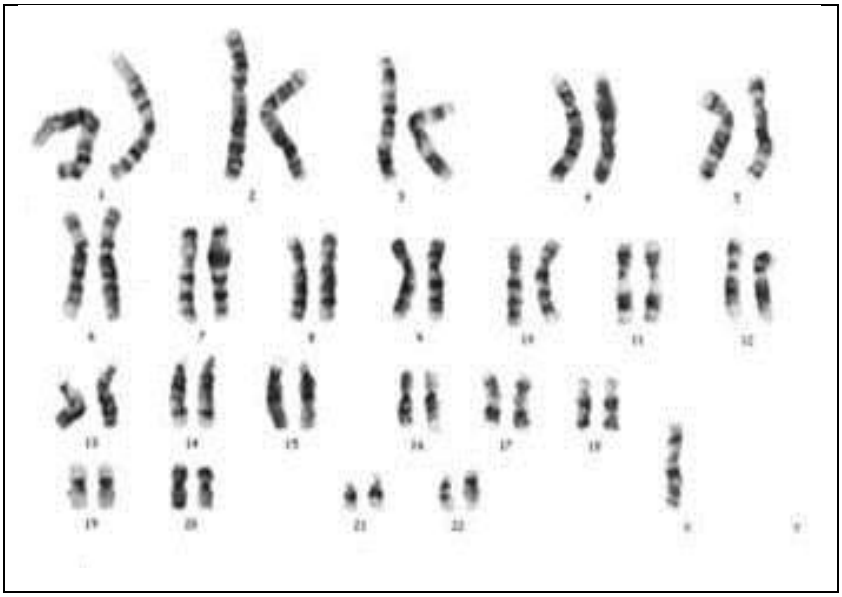

Figure 7. Karyotype result 45,X of patient no. 59

The patient present with PA, short stature, Tanner stage (1) absent axillary hair and webbed neck.

The distribution of diagnosis among 55 patients with female karyotype 46, XX revealed 14 patients with MRKH, two patients with CAH and one patient with pure gonadal dysgenesis, while the remaining 33 patients still with unknown causes.

According to the cytogenetic results of 18 patients with chromosomal abnormalities the diagnosis were Classical Turner syndrome in 8 patients, mosaic Turner in 9 patients and one patient with autosomal X translocation. The distribution of diagnosis among all patients showed in Figure 8.

The diagnosis of 6 patients with male karyotype 46, XY revealed CAIS in 2 patients, PAIS in one patient, 3 patients with pure gondal dysgenesis of undetermined cause.

Table 3. The karyotype results of 79 patients with primary amenorrhea

Chromosomal categories	***Karyotype***	***Number of patients***	
		n	***%***
Female Karyotype	46,XX	55	69.6%
Male karyotype	46, XY	6	7.6%
Numerical Abnormality			
Monosomy X	45,X	8	10.1%
Turners Mosaic	45,X/46,XX	3	3.8%
Presence of XY constitution			
	45, X/46,XY	2	2.5%
Structural Abnormality			
Marker chromosome	45,X/46,X +mar2%	1	1.3%
Isochromosome	45,X/46,X,iXq	3	3.8%
Translocation X;1	46,XX, t(1;X) (p34;q25)	1	1.3%

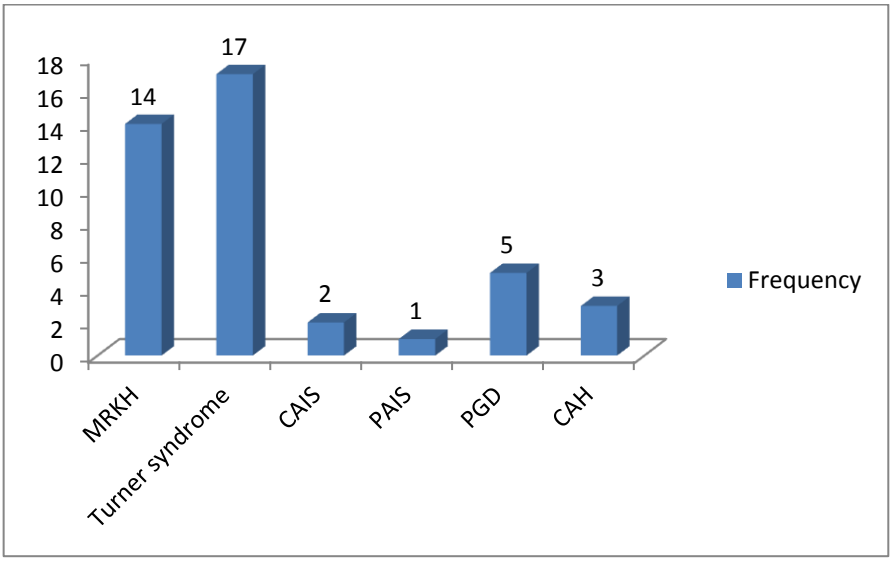

Figure 8. Frequency of diagnosis among 42 patients with primary amenorrhea

Clinical profiles

1. Age

Distribution of age revealed the mean age at referral was 23 years old. Most of patients in the age group (20 - 30) years, the youngest age was 16 years old and the oldest age was 35 years old. Table 4 show the distribution of age among 79 patients with primary amenorrhea.

Table 4. Distribution of age among primary amenorrhea patients

Age at referral	Primary amenorrhea	
	Frequency (n)	**Percentage (%)**
(16-20) years old	29	36.7%
(20– 30) years old	47	59.5%
(30-35) years old	3	3.8%
Total	79	100

2. Tanner stage

In this study the secondary sexual developement was measured by reveiwing the data of Tanner stage of the patients and the result was 55 patients with female karyotype 46, XX showed 26 (47%) patients with Tanner stage 5, and 11(20%) patients with stage 4, two (3.6%) patients with stage 3, four (7.2%) patients with stage 2 and 11(20%) patients with stage 1.

In patiets with male karyotype 46,XY there were 2 (28.5%) patients with stage 5, one (7%) patient with stage 3 and four (57.1%) patients with stage 1. In 18 patients with chromosomal abnormalities there were 12 (66.6%) patents with Tanner stage 1, two (11.1%) patients with stage 2, one (5.5%) patients with stage 3, one (5.5%) patient with stage 4 and two (11.1%) with stage 5.

3. Prader stage

The result of 55 patients with 46, XX karyotype majority of patients (54/55) had prader stage 0 and one patient with stage 4. In male karyotype

patients there were 2 patients with stage 0, four patients with stage 2 and one patient with stage 3. In the 18 patients with chromosomal abnormalities we detected 15 patients with Prader stage 0 and three patients with stage 2.

4. Other dysmorphic features

From the result of the dysmorphic features of patients with 46, XX karyotype there was 1 patient with Adams apple, 2 patinets with Hirsutism, one patient with wide spaced nipple, one patient with low setted ears and one patient with low posterior hair line.

In male karyotype 46, XY there were two patients with adams apple and one patient with sandal gap. The patient with translocation between chromosome 1 and X chromosome showed no other dysmorphic features rather than short stature. In turner syndrome patients we summaries the associated dysmorphic features in Table 5.

Table 5. Cytogenetic and clinical profile of primary amenorrhea with female karyotype 46, XX

N0	Age	Ht	Wt	TS	PS	AH	Other dysmorphic features	Radiological finding	Karyotype	Diagnosis
1	33	150	44	1	2	+	Adam's apple	N/A	46,XX	CAH
2	21	149	50	1	0	-	No dysmorphic features	No abnormality	46,XX	GD
3	16	156	47	5	0	+	N/A	N/A	46,XX	Unclassified
4	19	154	50	5	0	+	N/A	Uterine hypoplasia	46,XX	Unclassified
5	17	145	50	5	0	+	N/A	Uterine hypoplasia	46,XX	MRKH
6	25	156	53	5	0	+	N/A	N/A	46,XX	Unclassified
7	29	167	81	1	0	spare	N/A	N/A	46,XX	Unclassified
8	16	150	45	5	0	+	N/A	Uterine hypoplasia	46,XX	MRKH
9	19	159	50	5	0	+	No dysmorphic features	Uterine hypoplasia	46,XX	MRKH
10	18	139	40	5	0	+	N/A	N/A	46,XX	Unclassified
11	28	152	43	4	0	+	No dysmorphic features	No abnormality	46,XX	Unclassified
12	16	142	30	5	0	-	N/A	N/A	46,XX	MRKH
13	32	153	45	5	0	-	N/A	Uterine hypoplasia, vaginal agenesis	46,XX	MRKH
14	30	168	63	5	0	+	Low setted ears	Uterine hypoplasia, no cavity	46,XX	MRKH
15	23	150	50	5	0	+	N/A	Uterine hypoplasia	46,XX	MRKH
16	17	150	45	4	0	spare	N/A	Uterine hypoplasia	46,XX	MRKH
17	18	139	29	4	0	+	N/A	N/A	46,XX	Unclassified
18	19	143	43	5	0	+	N/A	No abnormality	46,XX	Unclassified
19	19	151	40	5	0	+	N/A	N/A	46,XX	Unclassified

20	35	155	70	5	0	+	No dysmorphic features	Uterine hypolpasia	46,XX	Unclassified
21	18	132	35	5	0	spare	N/A	N/A	46,XX	Unclassified
22	17	135	51	5	0	+	No dysmorphic features	N/A	46,XX	Unclassified
23	20	153	51	5	0	+	N/A	Uterine hypoplasia	46,XX	MRKH
24	19	151	49	4	0	+	N/A	N/A	46,XX	Unclassified
25	20	137	35	1	0	spare	N/A	N/A	46,XX	Unclassified
26	26	151	99	4	0	spare	N/A	Blind vagina	46,XX	MRKH
27	17	159	41	0	0	+	N/A	N/A	46,XX	Unclassified
28	19	156	44	1	0	spare	No dysmorphic features	Uterine agenesis	46,XX	Uterine a genesis
29	17	154	51	5	0	+	No dysmorphic features	N/A	46,XX	Unclassified
30	20	153	51	5	0	+	No dysmorphic features	Hypoplastic uterus	46,XX	MRKH
31	19	151	49	4	0	+	No dysmorphic features	Hypoplastic uterus	46,XX	MRKH
32	22	155	64	5	2	+	Hairsuitism	N/A	46,XX	CAH
33	19	126	62	2	0	+	N/A	N/A	46,XX	Unclassified
34	22	157	47	3	0	spare	N/A	Uterine hypoplasia	46,XX	MRKH
35	21	145	41	4	0	+	N/A	Uterine agenesis	46,XX	MRKH
36	22	155	50	4	0	+	N/A	Uterine hypoplasia	46,XX	MRKH
37	25	151	45	1	0	spare	N/A	Uterine agenesis	46,XX	MRKH
38	17	153	43	5	0	+	N/A	Uterine hypoplasia	46,XX	MRKH
39	17	148	43	2	4	spare	No dysmorphic features	N/A	46,XX	Unclassified
40	17	145	32	1	0	+	N/A	N/A	46,XX	Unclassified
41	26	149	34	1	0	spare	N/A	Uterine agenesis	46,XX	Uterine

										genesis
42	25	158	51	5	0	+	N/A	N/A	46,XX	MRKH
43	26	152	33	5	0	spare	N/A	N/A	46,XX	Unclassified
44	16	141	30	1	0	-	No dysmorphic features	N/A	46,XX	Unclassified
45	19	150	44	5	0	+	No dysmorphic features	N/A	46,XX	MRKH
46	20	152	52	1	0	spare	No dysmorphic features	N/A	46,XX	Unclassified
47	23	155	64	5	0	-	No dysmorphic features	N/A	46,XX	Unclassified
48	21	158	41	2	0	+	N/A	Uterine agenesis	46,XX	MRKH
49	20	151	44	1	0	spare	N/A	Uterine agenesis	46,XX	MRKH
50	16	150	45	4	0	spare	N/A	Vaginal agenesis	46,XX	MRKH
51	20	145	43	5	0	-	No dysmorphic features	N/A	46,XX	Unclassified
52	20	154	46	4	0	spare	No dysmorphic features	N/A	46,XX	Unclassified
53	31	149	56	4	0	-	Hairsuitism	N/A	46,XX	Unclassified
54	20	142	41	2	0	spare	No dysmorphic features	N/A	46,XX	Unclassified
55	19	149	35	3	0	spare	Low posterior hair line	N/A	46,XX	CAH

Ht= height Wt =weight PS= Prader stage TS= Tanner stage AH =axillary hair N/A= not available GD= gonadal dysgenesis

Table 6. Cytogenetic and clinical profile of primary amenorrhea patients with 46,XY karyotype

NO	Age	Ht	Wt	TS	PS	AH	Other dysmorphic features	Radiologic alfinding	Karyotype	Diagnosis
74	19	172	62	1	0	-	N/A	Uterine a genesis	46,XY	CAIS
76	24	164	45	1	3	spare	Adam's apple		46,XY	PAIS
77	23	157	59	1	2	+	N/A	Vaginal agenesis	46,XY	PGD
78	24	155.4	64.4	5	0	-	N/A	Uterine agenesis, and blind end vagina	46,XY	CAIS
79	26	167	66	3	2	-	Adam's apple	Uterine agenesis, testicular like structure in inguinal region	46,XY	PGD
80	24	168	69	1	2	-	Sandal gap	Uterine agensis	46,XY	PGD

Ht= height Wt= weight TS= Tanner stage PS= Prader stage AH= axillary hair N/A= not available PGD= pure gonadal dysgenesis

Table 7. Cytogenetic and clinical profile of 18 primary amenorrhea patients with chromosomal abnormalities

No	Age	Ht	Wt	TS	PS	AH	Other dysmorphic features	Radiological finding	Karyotype	Diagnosis
56	20	159	42	5	0	-	N/A	No abnormality	45,X(1%)/46XX(99%)	Mosaic Turner syndrome
57	20	146	40	5	2	-	No other dysmrphic features	N/A	45,X(90%)/46,XY(10%)	Mosaic Turner Syndrome
58	23	145	43	3	0	+	No other dysmrphic features	Hypoplastic uterus, no adnexa	45,X(20%)/46,XX(80%)	MosaicTurner Syndrome
59	20	136	38	1	0	-	Webbed neck/low posterior hair line	N/A	45,X	Classical Turner syndrome
60	19	136	29	1	0	spare	N/A	Uterine hypoplasia	45,X(2%)/46,XX(98%)	Mosaic Turner syndrome
61	21	135	29	3	0	-	Wide space nipple	No abnormality	46,X,iX(q10)(24%)/45X (76%)	Mosaic Turner syndrome
62	17	139	41	1	0	spare	Webbed neck/Low setted ears/Sheild chest/Low posterior hairline	No abnormality	45,X	Classical Turner syndrome
63	18	137	37	1	0	spare	Epicanthal fold/Short fourth metacarpal/Tappered fingers/Wide space nipple/webbed neck	Uterine hypoplasia	46,X,iX(q10)(10%)/45X(90%)	Mosaic Turner syndrome
64	23	142	56	1	0	-	Webbed neck/Low setted ears/Epicanthal fold/Tappered fingers/Wide space nipple/Sandel gap/Clinodactily scoliosis	Uterine hypoplasia	45,X	Classical Turner Syndrome
65	21	139	34	1	0	-	N/A	N/A	45,X	Classical Turner Syndrome
66	18	142	43	2	0	+	N/A	No abnormality	45,X	Classical Turner syndrome
67	26	145	39	1	2	spare	No other dysmrphic features	N/A	45,X(80%)/46,XY(20%)	Mosaic Turner syndrome
68	16	150	49	1	0	-	Low posterior hairline/Scoliosis	N/A	45,X	Classical Turner syndrome
69	21	144	26	1	2	-	No other dysmorphic features	N/A	46,XX,t(1;X)(p34;q25)	DSD
70	25	139	49	2	0	spare	Webbed neck/Low setted ears/Sheild chest/Cubitus valgus	No abnormality	46,X,i(X)(q10)(20%)/45,X(80%)	Mosaic Turner syndrome
71	16	140	35	1	0	spare	No other dysmrphic features	N/A	45,X	Classical Turner Syndrome
72	18	135	35	1	0	-	Webbes neck/cubitus valgus	N/A	45,X(98%)/46,X,+mar(2%)	Mosaic Turner syndrome
73	16	135	50	1	0	-	Webbed neck/Low setted ears/Wide space nipple	N/A	45,X	Classical Turner Syndrome

Ht= height Wt =weight PS= Prader stage TS= tanner stage N/A= not available

Table 8. Dysmorphic features associated with Turner syndrome

Dysmorphic features	**Classic (n=8)**	**mosaic (n=9)**
Craniofacial deformity		
Epicanthal fold	2 (25%)	1 (10%)
Puffy eye lids	0 (0.0%)	0 (0.0%)
Depressed nose	0 (0.0%)	0 (0.0%)
Low Posterior Hairline	2 (25%)	0 (0.0%)
High arched palate	0 (0.0%)	0 (0.0%)
Low setted ears	3 (37.5%)	1 (10%)
Neck deformity		
Short neck	0 (0.0%)	0 (0.0%)
Webbed neck	4 (25%)	3 (10%)
Chest deformity		
Sheild chest	1 (12.5%)	1 (10%)
Wide space nipple	2 (25%)	2 (20%)
Spine deformity		
Scoliosis	1 (12.5%)	0 (0.0%)
Extremities deformity		
Lymphoedema of hands and feets	0 (0.0%)	0 (0.0%)
Clinodactily	1 (12.5%)	0 (0.0%)
Short metacarpals	0 (0.0%)	1 (10%)
Tappered fingers	1 (12.5%)	1 (10%)
Cubitus valgus	0 (0.0%)	1 (10%)
Sandel gap	1 (12.5%)	0 (0.0%)
Semian crease	1 (12.5%)	0 (0.0%)
High waist to hip ratio	0 (0.0%)	0 (0.0%)
Ear infections or deafness	N/A	0 (0.0%)
Cardiac anomaly	0 (0.0%)	0 (0.0%)
Renal anomaly	N/A	N/A
Thyroid disorders		
Intellectual disability	0 (0.0%)	0 (0.0%)
Short stature	8 (100%)	7 (77.7%)

This result showed that the most common dysmorphic features associated with Turner syndrome was short stature, which had been seen in almost all of patients with classic Turner syndrome, in 7 out of 9 patients with mosaic Turner syndrome. Webbed neck had been seen

in 7 of patients, Epicanthal fold seen in 2 patients, low setted ears in 3 patients, wide spaced nipple in 2 patients, clinodactly in one patient, tappered finger in 1 patient, cubitus valgus in one patient, sandal gap in one patient, and scoliosis in one patient.

Table 9. Scoring system and the related karyrotype results

Score	Frequency of patients	Karyotype results
1	30	46,XX
	1	45,X(1%)/46.XX(99%)
	1	46,XY
2	25	46,XX
	5	46,XY
3	4	45,X
	1	45,X(20%)/46,XX(80%)
	1	45,X(2%)/46,XX(98%)
	1	45,X(90%)/46,XY(10%)
	1	45,X(80%)/46,XY(20%)
	1	46,XX,t(1;X)(p34;q25)
4	4	45,X
	1	46,X,iX(q10)(10%)/45X(90%)
	1	46,X,iX(q10)(24%)/45X(76%)
	1	46,X,iX(q10)(20%)/45X(80%)
	1	45,X(98%)/46,X,+mar(2%)

The result of scoring system and their related karyotype results revealed that under score 1 which is presented with primary amenorrhea only, there were 30 patients with female karyotype 46,XX, one patient with male karyotype 46,XY and one patient of mosaic Turner syndrome 45,X(1%)/46,XX(99%).

There were 25 patients with female karyotype 46,XX and 5 patients with male karyotype 46,XY matched score 2. Under Score 3 we demonstrated 4 patients with classical Turner syndrome(45,X), 4 patients with mosaic Turner and one patient with karyotype 46,XX,t(1;X)(p34;q25).

This study demonstrated 4 patients with classical Turner syndrome (45,X), three patients with isochromosme 46,X,iX(q10)/45X and one patient with marker chromosome 45,X(98%)/46,X,+mar(2%) matched score 4.