North American Open Medical Sciences & Medicine Research Journal
Vol. 3, No. 1, April 2016, pp. 1-17
Available online at http://narpub.com/Journals.php

Research article

Chromosomal profile in 1500 Sudanese Patients Suspected of having Chromosomal Abnormalities

Safa. M. Hamid [1*], Imad M. Fadl-Elmula [2], Sana.S Eltaher, MD, Ph.D[3]

[1]Department of Biochemistry and Molecular Biology, Faculty of Medicine Al Neelain University Khartoum, Sudan
[2]Department of Molecular biology and Clinical genetics, Faculty of Medicine, Al Neelain University, Khartoum, Sudan.
3 Sana.S Eltaher,MD,Ph.D Department of pathology, Faculty of Medicine, Al Neelain University, Khartoum, Sudan.

*Correspondence to: - **Safa. M. Hamid**, MSc, Ph.D. E-mail:- safamg2@hotmail.com.
P. O. Box, 12705, Code 11121 Khartoum-Sudan
Mobile phone: +249912288425 Office phone: +249155775075 Fax: +249183794422

Abstract

Introduction

Chromosomal abnormalities cause diverse functional problems to various organs and are frequently accompanied by developmental delay, growth, and endocrine disorders, mental retardation, dimorphism and infertility

Objectives

To evaluate the chromosomal changes in Sudanese patients referred for cytogenetic analysis and to compare our results with those reported elsewhere.

Material and Methods

A total of 1500 patients referred during 2009 and 2013 for cytogenetic to Cytogenetic Unit at Al Neelian Medical Research center, Faculty of Medicine, Al Neelian University, Sudan. The patients had various presentation including mental retardation, multiple congenital malformations, dysmorphic feature, primary and secondary amenorrhea, ambiguous genitalia and recurrent miscarriage. Cytogenetic analyses performed in peripheral blood samples that cultured in RPMI 1640 medium for three days. The clonality criteria and the karyotypic descriptions were according to the ISCN 2009 recommendations

Results

Of the 1500 patients investigated, 330 (22%) patients showed abnormal karyotypes and 1170 (78%) showed normal karyotypic findings. Out of the 330 patients with abnormal karyotypes, 310 (94%) patients showed numerical abnormalities whereas 20 (6%) patients revealed structural abnormalities. The most common karyotypic abnormalities were Down syndrome seen in 230 (74.1%) patients. Abnormalities, of sex chromosome seen in 69 (4.5%) of all patients of which 52 showed karyotype consistent with turner syndrome (16.7%), Nine patients were consistent with Klinefelter's syndrome, 3 patients consistent with triplex XXX, developmental of sexual diseases were seen in (5) patient (1.6%).

Conclusions

The present study, concluded that there is high incidence of chromosomal abnormalities most of them showed normal karyotype which was justifying the needs for cytogenetic analysis in patients with clinical suspicion.

Key words: Cytogenetic; Chromosomal abnormalities; Genetic counseling

Introduction

Chromosome abnormalities constitute a major category of medical genetic disorders, which are due to a change in the normal chromosome number or a change in the structure of a chromosome. They may involve one, two, or more chromosomes and may involve only part of a chromosome or the whole chromosome. Congenital anomalies, growth deficiency, and intellectual disability, mental retardation, or infertility; women with gonadal dysgenics spontaneous abortionists, and couples with repeated spontaneous miscarriages are findings often present in individuals with chromosome abnormalities, although some cytogenetic aberrations have little to no clinical effect. Approximately 1000 chromosome syndromes that make a major contribution to human morbidity and mortality have been reported so far (1;2). Chromosomal abnormalities affect at least 7.5% of all conceptions. Most of these abnormalities are spontaneously aborted and the frequency in live births is 0.6%. Several studies have shown documented chromosomal abnormalities among unselected populations of neonates and older children (3;4). Other cytogenetic studies among selected populations with abnormal phenotype features have also been conducted (5;6). The frequency of chromosomal abnormalities is known to be significantly higher in selected populations than in unselected populations (7;8). The increased awareness of the importance of chromosomal abnormalities as a cause of developmental delay, growth, and endocrine disorders, mental retardation, dismorphism and infertility has

generated an increased demand of cytogenetic studies. This has led to an increased recognition of many chromosomal disorders that otherwise would have been missed. However, we have noticed that some clinicians refer cases for cytogenetic study before exhausting other less expensive and time-consuming tests that may lead to the final diagnosis. In some instances, the patients were referred just to exclude the possibility of having an associated chromosomal abnormality (9).

Objectives:

The main objectives of this study are to evaluated the cytogenetic findings in Sudanese patient referred for suspected chromosomal anomalies that caused a variety of clinical disorders and to determined the commonest causes of requesting cytogenetic study, in addition to calculate the frequency of chromosomal aberration among the different groups of referrals.

Materials and Methods

One thousands five hundreds consecutive non-oncology cases, were referred to the Cytogenetic Unit at Al Neelian Medical Research center Al Neelian University, Faculty of Medicine Sudan, were included in this study. The age of the patients ranged from birth to 60 years.

For routine cytogenetic analysis, 0.3- ml peripheral blood samples were collected from the patients into heparinized test tubes, and then were incubated in complete lymphocyte culture medium (10% fetal bovine serum in RPMI-1640 with 0.15% phyto hem agglutinin and 1%Penstrept) in 5% CO2 incubator at 37 °C for 72h. Metaphases are harvested by adding colcemid for 45 min followed by hypotonic KCl treatment for 5 min and fixation using standard 3:1 methanol-acetic fixative (all the reagents were from Gibco Life Technologies Ltd., Paisley UK).A high-resolution study was done by synchronization using methotrexate (10–7*M*) for 17 h and thymidine (10–5*M*) for 5.5 h before harvesting, as mentioned elsewhere.

The karyotype of each patient was determined by G-banding using trypsin and Giemsa (GTG) technique according to Seabright M1971 (10), At least 30 cells were routinely analyzed; in cases of mosaics, this number was increased to approximately 100 metaphases. The best metaphases were photographed to determine the karyotypes. If the case was carrier of a translocation or an inversion or unusual karyotypes, their parents or other family members were also tested.

Cytovision imaging applied photography and karyotype were done for documentation in abnormal cases, the karyotypic descriptions were reported according to the International System for Human Cytogenetic Nomenclature recommendations ISCN, 2009(1) the relative frequency of each diagnostic group was calculated, and the percentage of abnormal cases and the distribution of the numerical and structural abnormalities were determined in each group. The frequencies were compared to similar studies using the Z test for Comparison of two frequencies with unequal variance. The findings in these cases are summarized in the Results section .A detailed interview was conducted

with all cases before cytogenetic analysis, and a detailed medical history was obtained. Informed consent for genetic testing was obtained from all patients.

Results

Of the 1500 patients investigated 330 (22%) patients showed abnormal karyotypes and 1170 (78%) showed normal findings. Of the abnormal karyotypes there were (310) patients 94% with numerical abnormalities, 20 patients (6%) with structural abnormalities and (17) patients1.5 % had normal karyotype result but had clinical finding that suspected of micro deletion syndrome.

For numerical abnormality (310) they classified into tow group according to the sex, male were 161 patient 48.8% female were169 patient 51.2% and for the Structure abnormality 20 patient male were 12 patient (66%) and female were 8 patient (44%). The ratio of female to male 3:2 , the patients were classified to 5 group according to their age, there was a peak of referred cases in the first 5 years of age (62.7% of patients), then the referred cases decreased in the ages between 6 and 15 years 68 patients (19.3%) After that the number of referrals decreased to a minimum at the age above 15 years 58 patients (18.5%).

According to the reason of referred (as stated on the request form) they classified to 11 group, The most common clinical reasons for performing cytogenetic dysmorphic features with developmental delay (29.49%), investigations were suspected Down syndrome (18.61%), short stature (12.62%), unclassified mental retardation (12.49%), multiple congenital anomalies (5.48%), abnormality in sexual differentiation (4.63%), recurrent miscarriage (4.21%), infertility (4.82%), amenorrhea (3.93%), suspected Klinefelter syndrome (2.22%), genetics counseling (1.5%) .

The rate of parental consanguinity among abnormal cases was 57.6%, mental retardation present in 85.9% of them, 72. 9% from the cases has no previous family history of chromosomal abnormality.

According to mother and father age they classified to 3 group , the more frequent mother age was the age above 40 years (153,47%) of patients and then the age from 30-40 years (144,43.6%) , the minimum frequency were present in the age from 20-30 years (31, 9.4%) Table (1) shows the demographic data of numerical abnormalities cases and table (2) shows the demographic data of structure abnormalities cases.

Table (1) the demographic data for numerical abnormality cases.

Variable		Frequency	Percentage
Sex	Male	149	49.0%
	Female	156	51.0%
Age	0-1 years	106	33.3%
	1-5 years	94	30.7%
	5-15 years	62	20.3%
	15-30 years	42	13.7%
	>30 years	6	2.0%
Mother age	20-30Years	231	9.5%
	30-40 Years	135	43.8%
	>40 years	144	46.7%
Father age	20-30 Years	36	11.4%
	30-40Years	138	44.1%
	>40 Years	136	44.4%
Consanguinity	Yes	175	56.9%
	No	135	43.1%
Family history	-ve	226	72.9%
	+ve	85	27.1%
Mental retardat	-ve	46	14.1%
	+ve	264	85.9%

Table (2) the demographic data of Structure abnormalities

		frequency	Percentage
Sex	Male	11	52.4%
	Female	10	47.6%
Age	0-1 years	5	23.8%
	1-5 years	6	28.6%
	5-15 years	4	19.0%
	15-30 years	4	19.0%
	>30 years	2	9.5%
Mother age	20-30Years	1	4.8%
	30-40 Years	10	47.6%
	>40 years	10	47.6%
Father age	20-30 Years	0	0.0%
	30-40Years	8	38.1%
	>40 Years	13	61.9%
Consanguinity	Yes	13	61.9%
	No	8	38.1%
Family history	-ve	21	100.0%
	+ve	0	0.0%
Mental retardation	-ve	3	14.3%
	+ve	18	85.7%

From numerical abnormalities two hundred and thirty cases (127 males and 103 females) male to female ratio, (1.2:1) included in this study were cytogenetically confirmed cases with a clinical diagnosis of Down syndrome the rate of parental consanguinity among dawns syndrome in this study is (34.7%). The median maternal age at the time of birth of the affected child was 37.8 years old mother age was above 40 year found in 113 patient (49.6%), from 30-40 years found in 105 patient(45.2%) and the lowest percentage was found in the age of (20-30)year 12 patient (5.3%), The average age at presentation was 15.6 months (range 1 days–13years) 120 patients (52%) of the cases were of first and second birth orders distributed as flow :nondisjunction 112 patient (50% from the total nondisjunction) translocation 4 patients (67%) from the total translocation , 2 patient mosaics (66%) out of the total mosaics number , 43.9% of the cases had Congenital heart disease The most common cardiac defects observed were ventricular septal defect (17.%) and atrial septal defect (15%) , among the all cases 85.3% from the cases has no previous family history of chromosomal abnormality while the 14.7% show the previous cases of chromosomal abnormality, 221 patients (96.08%) were found to have non-disjunction trisomy21 and 6 patients (2.6 %) with translocation with ratio of F: M was 2:1, Mosaics was 3 patient (1.3%) with ratio of men to female 2:1, Table (3) shows the frequency of dawn syndrome, nondisjunction was the most common type of abnormality, followed by translocation and lastly mosaic respectively .

Table (3) the frequency of down syndromes

Karyotype	Observed N	Percentage
46,XX t (21;14)	4	1.7%
46XY t (21;14)	1	0.43%
46XY t (21.21)	1	0.43%
47,XX +21	86	37.3%
47,XY +21	135	58.6%
47,XY +21/46,XY	2	0.86%
47,XX +21/46,XX	1	0.43%
Total	230	100%

Abnormalities of chromosome 18 (47XY+18) were seen in 8 patients (2.6%) the Mother age of trisomy 18 in 5 patient (62.5%) from 30-40 years , 3 patient (37.5%) their mother age were above 40 years, parental consanguinity was found in 4 patient (50%). The family history of previous chromosomal abnormality was found in one patient other 7 patient have no any previous history of chromosomal abnormality in their families, The Abnormalities of chromosome13 (47XY+13) were observed in two patients of present study (0.6%), parental consanguinity was found in 1 patient (50%) and The family history of previous chromosomal abnormality was not found in both of them.

Abnormalities of sex chromosome were seen in (69) patients 20.9% from total number of numerical disorder, distributed as flow, the most frequent sex chromosomal abnormality was turners syndrome (45X) was found in (52) patient (15.7%), triplex XXX syndrome were found in 3 patient 0.90% klinfilter syndrome in 9 patient (2.7%), among cases with Klinefelter's syndrome, the classic karyotype (47, XXY) was common. Other 5 cases had discordance between the chromosomal sex and the phenotype (1.5%) , Turners syndrome referred with different reason short stature 43 patient 82.7%, dysmorfic feature in 5 patient (9.6%) , primary Amenorrhea 4 patient (7,7%) , their mother age were show the peak of cases in the age above 40 year(42.3%) after that the age from 30 to 40 year (32.7%) the lowest age was from 20 to 30 years (25%) the parental consanguinity were found in 26 patient (50%), the previous family history of chromosomal abnormality in their families was not found in (82.7%) of cases while in (17.3%) of patient we found history of chromosomal abnormality, mental retardation were present in (67%) of cases.

Abnormalities of Other chromosome were seen in 7 patients. (1.6%) distributed as flow (47xy+4), (47xx+9), (47xy+22), (47xy+14), (47xx+3), (47xx+16), in the present study one newborn infants had polypoid.

Structure abnormalities found in 20 patient 12 male (66%) and 8 female (44%) The ratio of female to male 3:2 their karyotype result show deletion in 8 patient (40%) inversion in 2 patient (10%) translocation in 7 patient (35%) fragile X in 3 patient (15%) patient ,54% from patient their mother age above 40 year, (41%) of patient their mother age 30-40year one patient (5%) his mother age 20.30 year ,the age of patient ranged from 0-1found in 5 patient (22.7%),from 1-5 year in7 patient (31.3%) in 3 patient(22.7%) their age from 5-15year, in the age from 15-30 year 3 patient(13,6%) above 30year 2 patient(9.1%) the majority of them were refer with dismorfic features(50%) and the other with variable reason repeated abortion , developmental delay and other reason, the parental consanguinity were found in 58.8% of patient ,just in tow patient (8.3%) we found previous family history of chromosomal abnormality while in 91.6% of the cases the previous family history of chromosomal abnormality was not found , 79.2% of patient has mental retardation and in 5 patients (20,8%) mental retardation was not present,the demographic data of Structure abnormalities cases where resented in Table (2) , Table (4) shows Karyotpe result for all abnormal cases using conventional cytogenetic technique, Figure (1) shows the diagnosis Distribution of numerical abnormality cases , Figure (2) shows distribution of mother age with number of cases among categories of type of abnormality

This study resulting that the number of patients' associated with mental retardation was significantly higher (282, 85.5%) than the number of patients without mental retardation (48, 14.5%), the p-value of goodness of fit using chi-square test (0. 000) those patients were characterized by:-

The most frequent type of abnormality was numerical abnormality (263, 93%) structure abnormality (19, 7.7%) the p-value of goodness of fit (0.000).

The ratio of male: females were 1:.94 which mean that the number of male to female was insignificantly higher than females. The p-value of goodness of fit (.634).

Te most significantly affected group of age was the group from 0-1 year (103, 36. 5%), the p-value of goodness of fit (0.000).

The degree of parental consanguinity among them was significantly more frequent (160, 56.7%) The p-value of goodness of fit (0.024).

Most of them were significantly without previous family history of chromosomal abnormality (215, 76.2%) and those with previous family history (67, 23.8%) The p-value of goodness of fit (0.000).

There were two types karyotype result appear more frequent than the other this karyotype were down syndrome (216,76%),turner syndrome (35,12%) the remaining 31 cases distributed to the other karyotype result The p-value of goodness of fit (0.000).

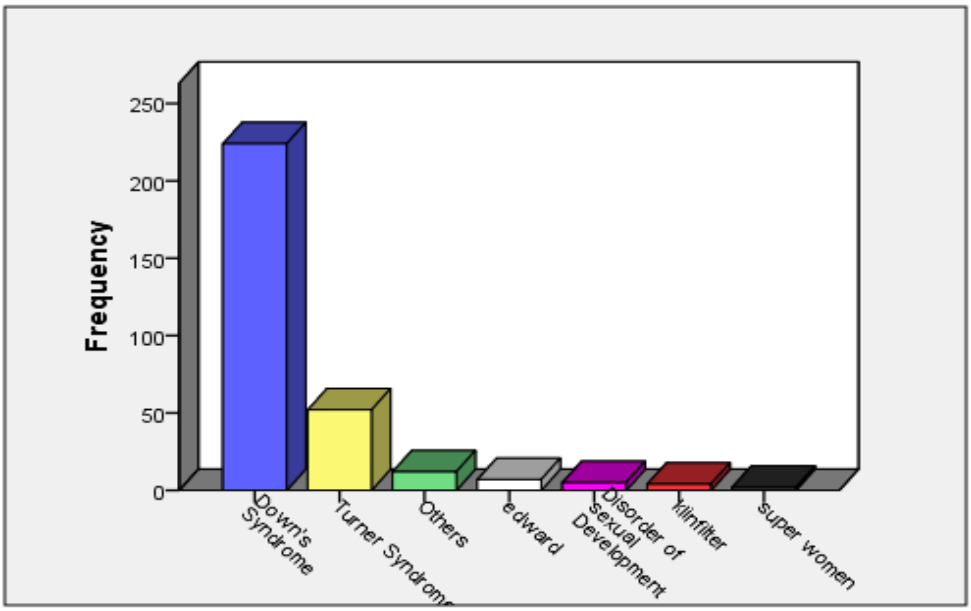

Figure (1) Distribution of study population according to numerical abnormalities

Table (4) Frequency and percentage of Karyotpe of abnormal cases

Karyotype_Results	Frequency	Valid Percent
46,XY	2	.6
46,XX	3	.9
45,X	52	15.8
46,XY del (4) p(16)	2	.6
46,X,?inv(Y)(q11;q12),t(14;21)(p13;p10)	1	.3
46,XX T(21;14)	4	1.2
46,XX del(22), q11	3	.9
46,XY T(22;9)	1	.3
46,XY T(21;21)	1	.3
46,XY T(21;14)	1	.3
46,XY del(13),q12	1	.3
47,XXY	9	2.7
47,XXX	3	.9
47,XX +21	86	26.1
47,XY +21	135	40.9
47,XY +18	8	2.4
47,XY +13	2	.6
47,XY +21/46,XY	2	.6

47,XX +21/46,XX	1	.3
46y,fra(x)(q27.3)	3	.9
47xy+4	2	.6
45xy-2	1	.3
47xxinv16+22	1	.3
47xy+6del(12)(p(13)	2	.6
47xx+9	3	.9
47xy+22	1	.3
Total	330	100.0

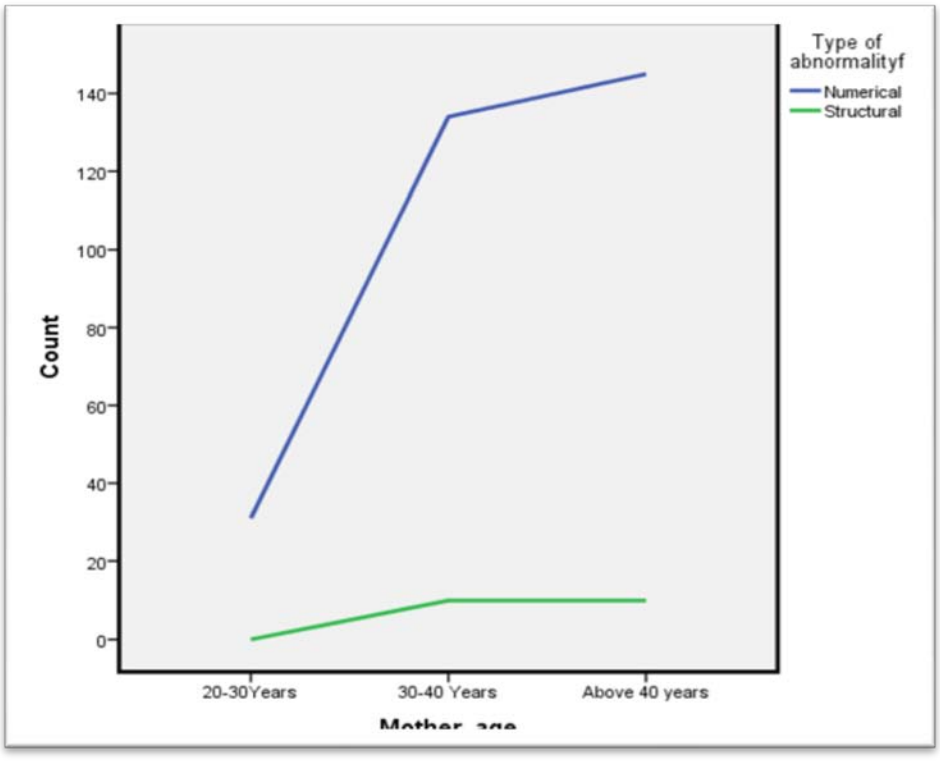

Figure (2) Distribution of mother age with number of cases among categories of Type of abnormality

Discussion

This study was done to evaluate the pattern of cytogenetic in Sudan, and to determine the frequency of chromosomal abnormalities in the different groups. Cytogenetic analysis services were recently established in Sudan. This may reflect low awareness of the physicians, families as well as health-care providers for early suspicion of affected newborns. The diagnosis of chromosomal abnormity is not practiced in Sudan long time ago; this could be attributed to the lack of awareness, specific policy, and guidelines.

There were wide variations in the frequency of chromosomal aberrations in individuals suspected of having genetic disorders as reported by different investigators (8;11). In the present work, chromosomal aberrations were detected in (22%) of the cases with suspected genetic disorders Similar frequencies have been reported previously in other studies, including Mitra (1988) studied 325 patients and found chromosomal aberrations in 77 patient (23.6%) (12) , Hatem and Jamil (2002) studied 747 patients and found chromosomal aberrations in 152 (20.3%). (13) Al-Awadi et al. studied 472 patients and found 92 cases (19.5%) (14). Al-Arrayed reported a frequency of 27% among 500 patients (15), Verma and Dosik found a frequency of (27.1%) among 357 patients (6) and Singh reported a frequency of(28.8%) among 451 patient(5) Mallana T. Goud, reported a frequency of 510 (28.3%) among1800 patients (2) Aboussair N. studied 5572 patients and found chromosomal aberrations in 1504 (27%) (16) but it was higher than(15.8%) that reported by Berry et al. studied 114 patients and found chromosomal aberrations in 18 patients , Navsaria et al. evaluated 1000 patients and found chromosomal aberrations in 160 (16%) (17).and Muneera Al Husaina Osama K. Zakib studied1000 patients found chromosomal aberrations in 134 (13.4%) (18) ,but its lower than Winter et al (1980) studied 140 patients and found chromosomal aberrations in 60 (43%).(19) , Shah et al 1990 reported a frequency of(39.6%) of abnormality, Mohamed M. Mokhtar 1997 studied137 patients chromosomal aberrations were detected in 53 patients (38.7%)(2), Kenue et al. among 120 patients chromosomal aberrations were detected in 48 patients (40%) (20) M. Balkan reported a frequency of (32.2%) among4216 patients (21) Vasilica Plăiaşu 2012.amang 592 patients chromosomal aberrations were detected in 321 (54.2%) patients, .

This study found that two groups of referrals (couples with short stature and patients with dysmorphic features) account to more than 50% of the cases. The next most common referrals were those with Primary Amenorrhea, repeated abortion, developmental delay, Disorders of sexual Development, Ambiguous genitalia, delayed milestones, infertility, cases suspected to have fragile X, Cerebral Palsy and cases for genetic counseling.

.In the current study Down syndrome forms the most frequent autosomal chromosomal abnormalities among patients with abnormal chromosomes; Down syndrome was identified especially in males which observed a similar gender ratio as 54.6% males by Duarte et al. 2004, and 53.1% males by M. Balkan of the Down's cases.

The frequency of Down syndrome in this value is agree with 67.9%, that reported by Mokhtar, 1997, 76.7% by Goud et al, 72.80% by Nisrine Aboussair 2011, 81% by Vasilica Plaiasu1 2012 , but it was lower than 85% reported

by zaki1999, 88.6% M. Balkan, 91%Shaikha Al arrayed This could be attributed to its easy detection at the clinical level.

Frequency of regular trisomy 21 was range from 84.6-95%. (22) n present study the frequency of regular trisomy is similar to Nisrine Aboussair 96%, Goud *et al* 95.7%, 91.93Vasilica Plaiasu1, agreeing with other surveys, which range from 84.6-95%. (22)The frequency of translocation dawns syndrome was 2.6% with ratio of F::M 2:1which it was little less when compared with 3% by Al arrayed ,3.1%, by Goud and 6.15% by Vasilica Plaiasu1, also the previous reports of 8.3%,28 5.6%,35 5.2%,36 and 6.8%.37 47, +21/46, are higher than our result. Mosaics accounted for 2-3% (22) but the present study found 1.3% with ratio of men to female 2:1 it similar to1.3% by Goud *et al*, and 1.42% Aboussair and 1.57 %by Vasilica Plaiasu1,we found only one cases combination mosaic and translocation(46xy.46xy t (14.21) this cause from father of patient with translocation (14.21).

Although it is well known that consanguinity increases the risk to offspring, particularly for autosomal recessive conditions, the definite effect of consanguinity on chromosomal abnormality is unknown (21). Some authors postulate a direct relationship of consanguinity with a higher incidence of dawn syndrome, (22).which is agree with the finding of this study.

.In the present study, Trisomy 18 and Trisomy 13formed the 2nd and 3rd largest Trisomy groups this result was compactable with(2.2%)of trisomy 18 and(0.7%), of trisomy 13 by Mohamed M. Mokhtar, 1,8% for Trisomy 18 and1.1%of Trisomy 13by Goud and1.55% of Trisomy 13and1.25%of Trisomy 18 by Vasilica Plaiasu1 But it was low when compare with 4% of Shaikha Al arrayed for Trisomy 18 and Trisomy 13.The reduced frequency of cases with this chromosomal abnormality may be explained by the fact that most fetuses with trisomy 18 are spontaneously eliminated prenatally (23) and that Edwards syndrome is a fatal outcome in most cases .

The most fetuses with trisomy 18 are spontaneously aborted (24). When the pregnancy is brought to term, the post-natal lifetime is limited to one or two months in 80% of the cases, except when there is somatic mosaicism (21).Only two cases were identified as having Patau's syndrome. This syndrome is well known for its low life expectancy and the well-defined features that allow an early diagnosis in the first days of life, except in cases of mosaicism , The small number of cases diagnosed with Patau syndrome may be explained first by the fact that many fetuses with this chromosomal abnormality stop in evolution, trisomy 13 occurring in approximately 2% of spontaneous abortions in the first trimester, representing the fourth most common cause of autosomal trisomy, after trisomies of chromosomes16, 21 and 22 (25).

Our patients' age was twenty days and 8 days, the mosaicism was not observed in this individual.

Numerical chromosomal abnormalities involving the sex chromosomes in the current study were higher than 2.8% reported by Goud, 2.9%by Mokhtar and similar to (3.95%) by Nisrine Aboussair,. This percentage is in agreement with other surveys and is mainly due to the fact that a sex chromosome imbalance has a much less deleterious effect on the phenotype than autosomal aneuploidy (16) the most frequent were Turner s syndrome (76.4%) patients, (13.2%) with Klinefelter syndrome and (5.8 %) with trisomy X. Among cases with Klinefelter's syndrome, the

classic karyotype (47, XXY) was common other 5 cases (7.2%) had discordance between the chromosomal sex and the phenotype.

Turner's syndrome is a total or partial X chromosome monosomy. It affects one in 2500 live-birth in women (16) it is caused by partial or complete absence of a chromosome X **,** it is one of the few chromosomal aberrations that can be recognized clinically during infancy or childhood based on short stature, broad shield chest, lymphoedema of the lower limbs, webbed neck and multiple minor anomalies However, karyotyping is necessary to confirm the diagnosis ,

. The present study showed homogeneous monosomy 45, X as the most frequent anomaly cases Other abnormalities 45X/46 XX found only in 2 patients This frequency agrees with Guera et al. (18%) but it was lower than,10.8% that reported by M. Balkan1 (21) 2.7% by Goud and 8,11 % by Nisrine , 2.9% mochtar ,2.5% Kenue et al. (20) Shaikha Al arrayed3.09% Vasilica Plaiasu1,2.8%, Triploidy is a common finding in spontaneously aborted products of conception, but rare in live born infants. (26),in this study we found one newborn with triploidy this was agreement with Goud 2004(27)

Different structural chromosomal abnormalities were recorded ,the current study it similar to 6.7%Goud(2), 5.1% Al Husain/Zaki ,5.6% Mohamed M. Mokhtar but it lower than 11.21%by Vasilica Plăiaşu1**,** 20% by buklan, 27.6%by Shaikha Al arrayed and higher than 2.45% Nisrine Aboussai, For structural autosomal chromosome aberrations, deletion was the most common (33.3%), translocation 29% ,fragile X (12.54%) inversion 8.3% followed in order of frequency .

Conclusion

This study concluded that high rate of chromosomal abnormalities was found in the study population demonstrate the importance of cytogenetic evaluation in patients who are clinically abnormal. This type of study provides a basis for determining the risks of recurrence and for deciding on clinical treatment and genetic counseling also showed that the pattern of referrals of cases for cytogenetic study and the frequency of chromosomal aberrations in those cases generally conform to those reported in similar studies. Thorough clinical search for subtle dysmorphic features should help physicians to decide on the need to request cytogenetic study. Referral of cases to an experienced dysmorphologist prior to cytogenetic study is advisable. This will decrease the number of unnecessary referrals and enhance the referrals of cases with minimal features of chromosomal anomalies.

Disclosure of Benefit: - The authors declare that they have no conflicting interests, and the present work was not supported and/or funded by any Drug Company.

References

(1) Brothman AR, Persons DL, Shaffer LG. Nomenclature evolution: Changes in the ISCN from the 2005 to the 2009 edition. Cytogenet Genome Res 2009;127(1):1-4.

(2) Goud MT, Al-Harassi SM, Al-Khalili SA, Al-Salmani KK, Al-Busaidy SM, Rajab A. Incidence of chromosome abnormalities in the Sultanate of Oman. Saudi Med J 2005 Dec;26(12):1951-7.

(3) Tatic A, Vasilica M, Colita A, Vasilache D, Dobrea C, Jardan C, et al. Refractory anemia with ringed sideroblasts and thrombocytosis without JAK2 V617F mutation: report of three cases. Rom J Morphol Embryol 2013;54(4):1177-82.

(4) Wanzer SH, Adelstein SJ, Cranford RE, Federman DD, Hook ED, Moertel CG, et al. The physician's responsibility toward hopelessly ill patients. N Engl J Med 1984 Apr 12;310(15):955-9.

(5) Singh DN. Cytogenetic study of individuals suspected of chromosome anomalies. Clin Pediatr (Phila) 1977 Jul;16(7):619-22.

(6) Verma RS, Dosik H. Incidence of major chromosomal abnormalities in a referred population for suspected chromosomal aberrations: a report of 357 cases. Clin Genet 1980 May;17(5):305-8.

(7) Shah VC, Murthy DS, Murthy SK. Cytogenetic studies in a population suspected to have chromosomal abnormalities. Indian J Pediatr 1990 Mar;57(2):235-43.

(8) Nkanza NK, Tobani CT. Chromosomal abnormalities: experience at Harare Hospital. East Afr Med J 1991 Aug;68(8):611-6.

(9) Al HM, Zaki OK. A survey of 1,000 cases referred for cytogenetic study to King Khalid University Hospital, Saudi Arabia. Hum Hered 1999 Jul;49(4):208-14.

(10) Seabright M. High resolution studies on the pattern of induced exchanges in the human karyotype. Chromosoma 1973;40(4):333-46.

(11) Shah VC, Murthy DS, Murthy SK. Cytogenetic studies in a population suspected to have chromosomal abnormalities. Indian J Pediatr 1990 Mar;57(2):235-43.

(12) Mita AB, Murty VV, Pratap M, Sharma A, Sharma JK, Das BC. Chromosome abnormalities in referred patients--a five year study. Indian J Med Res 1988 May;87:475-8.

(13) El-Shanti H, Al-Alami J. The pattern of peripheral blood chromosomal abnormalities in Northern Jordan. Saudi Med J 2002 Dec;23(12):1552-4.

(14) Al-Awadi SA, Teebi AS, Sundareshan TS. Complex chromosomal rearrangement involving chromosomes 11, 13, 14 and 18 resulting in monosomy for 13q32----qter. Ann Genet 1985;28(3):181-4.

(15) Al-Arrayed SS. Review of the spectrum of genetic diseases in Bahrain. East Mediterr Health J 1999 Nov;5(6):1114-20.

(16) Aboussair N, Jaouad IC, Dequaqui SC, Sbiti A, Elkerch F, Yahya B, et al. Cytogenetic analysis of 5572 patients referred for suspected chromosomal abnormalities in Morocco. Genet Test Mol Biomarkers 2012 Jun;16(6):569-73.

(17) Navsaria D, Mathews T, Conte RA, Verma RS. Chromosomal anomalies in 1,000 children referred with suspected genetic disorders. Hum Hered 1993 May;43(3):137-40.

(18) Al HM, Zaki OK. A survey of 1,000 cases referred for cytogenetic study to King Khalid University Hospital, Saudi Arabia. Hum Hered 1999 Jul;49(4):208-14.

(19) Winter RM, Ridler MA, McKeown JA. A diagnostic survey of infants referred for chromosome analysis in the neonatal period. Br Med J 1980 Oct 18;281(6247):1045-7.

(20) Kenue RK, Raj AK, Harris PF, el-Bualy MS. Cytogenetic analysis of children suspected of chromosomal abnormalities. J Trop Pediatr 1995 Apr;41(2):77-80.

(21) Balkan M, Akbas H, Isi H, Oral D, Turkyilmaz A, Kalkanli S, et al. Cytogenetic analysis of 4216 patients referred for suspected chromosomal abnormalities in Southeast Turkey. Genet Mol Res 2010;9(2):1094-103.

(22) Goud MT, Al-Harassi SM, Al-Khalili SA, Al-Salmani KK, Al-Busaidy SM, Rajab A. Incidence of chromosome abnormalities in the Sultanate of Oman. Saudi Med J 2005 Dec;26(12):1951-7.

(23) Giaccardi A, Sardi R, Priora U, Vivalda M, Domeneghetti G, Girone P. [Trisomy 18 or Edwards' syndrome. A report of 4 clinical cases]. Minerva Pediatr 1991 Apr;43(4):343-9.

(24) Giaccardi A, Sardi R, Priora U, Vivalda M, Domeneghetti G, Girone P. [Trisomy 18 or Edwards' syndrome. A report of 4 clinical cases]. Minerva Pediatr 1991 Apr;43(4):343-9.

(25) Jacobs PA, Hassold TJ, Henry A, Pettay D, Takaesu N. Trisomy 13 ascertained in a survey of spontaneous abortions. J Med Genet 1987 Dec;24(12):721-4.

(26) Patil SR, Lubs HA, Brown J, Cohen M, Gerald P, Hecht F, et al. Incidence of major chromosome abnormalities in children. Cytogenet Cell Genet 1977;18(5):3102-6.

(27) Goud MT, Al-Harassi SM, Al-Khalili SA, Al-Salmani KK, Al-Busaidy SM, Rajab A. Incidence of chromosome abnormalities in the Sultanate of Oman. Saudi Med J 2005 Dec;26(12):1951-7.