International Journal of Anatomy and Research,
Int J Anat Res 2017, Vol 5(4.3):4716-22. ISSN 2321-4287
DOI: https://dx.doi.org/10.16965/ijar.2017.456

Original Research Article

CYTOGENETIC STUDY IN COUPLES WITH BAD OBSTETRIC HISTORY

Vidya H K *[1], B S Suresh [2].

[*1] Assistant Professor, Department Of Anatomy, Shridevi Institution Of Medical Sciences And Research Hospital, Tumkur, Karnataka, India.

[2] Professor, Department Of Anatomy, Sri Siddhartha Medical College, Tumkur, Karnataka, India.

ABSTRACT

Background: Bad obstetric history (BOH) implies previous unfavorable fetal outcome. In couples with bad obstetric history percentage of chromosomal abnormalities varies from

1-25% for individuals. Hence cytogenetic evaluation helps to detect any chromosome defects. This study was done to correlate chromosomal variations with bad obstetric history.

Objective: To study the relation between bad obstetric history and associated chromosomal abnormalities. To study different types of chromosomal abnormalities associated with the bad obstetric history

Materials and Methods: In the present study 60 couples with bad obstetric history were taken up for the study. After taking informed consent, the history and clinical features were noted. Karyotyping was done using standard procedures. Investigations were done to diagnose other associated conditions and were referred to the proper centers for further evaluation and management.

Results: The study was conducted on 60 couples with bad obstetric history, and the following results were obtained. Out of 168 pregnancy losses, 59% of pregnancy loss were in 1st trimester, 17% in second trimester, 12% were IUD's, 2% were still born, 10% others like died after birth or with congenital anomalies etc…. 17 anomaly cases were recorded in antenatal scan. 24 couples had the history of consanguineous marriage. Cytogenetic evaluation showed . 57 were normal male, 55 were normal female, 4 normal variations, 1 inversion and 2 translocations.

Conclusion: Karyotype analysis in couples with bad obstetric history helps in finding any chromosomal abnormalities, which inturn helps in identification of chromosomal abnormality as the etiology, facilitates genetic counseling and appropriate management.

KEY WORDS: Bad obstetric history ;congenital anomalies; Karyotype; consanguinity; balanced translocation; Robertsonian translocation; mosaicism; inversion; chromosomal variation, genetic counseling.

Address for Correspondence: Dr.Vidya H K, Assistant Professor, Department Of Anatomy, Shridevi Institution Of Medical Sciences And Research Hospital, Tumkur-572106, Karnataka, India.
E-Mail: vidyassmc@gmail.com

Access this Article online

Quick Response code

DOI: 10.16965/ijar.2017.456

Web site: International Journal of Anatomy and Research
ISSN 2321-4287
www.ijmhr.org/ijar.htm

Received: 23 Sep 2017
Peer Review: 26 Sep 2017
Revised: None

Accepted: 08 Nov 2017
Published (O): 01 Dec 2017
Published (P): 01 Dec 2017

INTRODUCTION

All conceptions do not result in live births. Bad obstetric history (BOH) implies previous unfavorable fetal outcome in terms of two or more consecutive abortions, early neonatal deaths still births, intra-uterine fetal death, intra-uterine growth retardation and congenital anomalies. [1]. Pregnancy loss can be defined as the unexpected and unplanned spontaneous loss of a pregnancy before the fetus is capable

of extra-uterine survival [2]. Pregnancy losses are more common among morphologically abnormal embryos [3]. For any given pregnancy the reported risk of pregnancy loss is 15% and likelihood of consecutive three losses would be 0.34%. [4].

A high proportion of early miscarriages have been found to have a chromosomal abnormality, approximately 50% in 1st trimester and 20% in 2nd trimester [5]. Recurrent miscarriage has been directly associated with parental chromosomal anomalies, maternal thrombophilic disorders and structural uterine anomalies and indirectly with maternal immune dysfunction and endocrine abnormalities [6].

In couples with bad obstetric history the percentage of chromosomal abnormalities varies from 1-25% for individuals, the most common chromosomal rearrangement is balanced reciprocal or Robertsonian translocation which may lead to unbalanced translocations in the fetus, resulting in miscarriage. Other chromosomal abnormalities seen usually are sex chromosome mosaicism, inversion and ring chromosome [7].

In couples with chromosome defects cytogenetic examination of both partners will be helpful in predicting recurrence as wll as forming basis for genetic counseling [6].

In the present study 60 couples with bad obstetric history were evaluated for any chromosomal abnormalities by karyotype analysis of their peripheral blood.

MATERIALS AND METHODS

In the present study, 60 couples with Bad obstetric history attending OP/ IP in the departments of OBG, Sri Siddhartha Medical College, Tumkur in between February 2011 to January 2013. (Period of 2 years) were selected. After taking ethical committee clearance, Informed consent was taken and history regarding couples age, address was recorded. Emphasis was laid on history of consanguineous marriage among couples, age at 1st conception, obstetric history, and menstrual history. A brief general and systemic examination of the couple were done, any significant finding were documented. Karyotyping of the couples was done. The preparation of the chromosomes for karyotyping was as follows: About 2ml of heparinized blood was collected from peripheral veins. Lymphocytes were grown in RPMI 1640 culture and 15 % serum supplemention. Phytohemaglutinin (PHA) was added as the mitotic stimulant (0.5 ml of the innoculum) and the samples were incubated for 72 hours at 37^0C in carbon dioxide incubator. The cells were arrested at metaphase with 0.1% colchicines. Hypotonic treatment was done and cells were fixed with 3 changes of fixative (3:1, methanol: acetic acid). The prepared slides were stained with GTG (G-band using Trypsin and Geimsa stain). Chromosomal analysis was done under 100x, magnification. Overall. 15 metaphase spreads were screened and 5 metaphases were captured using a CCD camera. The captured picture was further enhanced by adjusting the sharpness, brightness and contrast and the printout was taken. According to ISCN 1995 standards.

Karyotyping was done to detect any structural and numerical abnormalities. The couples were advised genetic counseling. Follow up of the couples was done on regular basis.

Inclusive Criteria's for selection of couples: Couples with history of 2 or more recurrent abortions/ stillbirths/ intrauterine deaths/congenital anomalies were included.

Exclussive Criteria's for selection of couples: Couples with less than 2 recurrent spontaneous pregnancy loss Couples with any other illnesses causing BOH, were excluded from the study.

RESULTS

Pregnancy loss at different duration of pregnancy: Among 60 couples with BOH totally 168 pregnancy were lost, out of which more than 50% pregnancy loss are in the first trimester,16% in second trimester, 2% are stillborn, 12% are IUDS, 10% others.

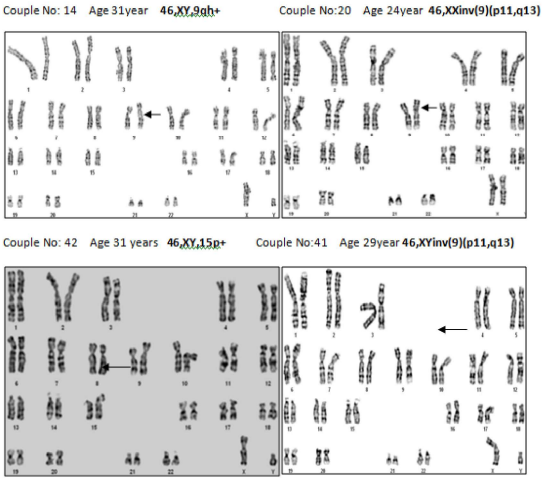
Among 3 couples with chromosomal abnormality there were 8 pregnancy loss, out of which 4(50%) in 1st trimester, 2(25%) in 2nd trimester and 2(25%) IUDS, out of 8 pregnancy loss, couples with reciprocal translocation had 3 pregnancy losses in the 1st trimester, couple with Robertsonian translocation had 1in 1st trimester and 2 in 2nd trimester. Couple with inversion of chromosome 6 had 2 IUD's. Among two individuals with inversion of chromosome 9, there were 6 pregnancy losses out which 5 were in

the 1st trimester and 1 in second trimester. In couple with 9qh+ had 2 pregnancy loss in the 2nd trimester with antenatal detection of poly-cystic kidney in both pregnancy losses.

Karyotype results of couples with BOH: In the present study karyotyping of 60 couples with bad obstetric history were done , out of 120 Karyo-type Normal 46,XY – 57, Normal 46,XX – 56

Normal Variations –4
46,XY,9qh+,
46,XY,15p+,
46,XX,inv(9)(p11q13),
46XY,inv(9)(p11q13)

Fig. 1. Karyotypes showing normal variations.



Abnormal variation -3
Inversion :- 46,XX,inv(6)(p22q13)
Reciprocal translocation:-46,XX,t(3;4)(p13;q33)
Robertsonian translocation :
- 45,XX,der(14;21)(q10;q10)

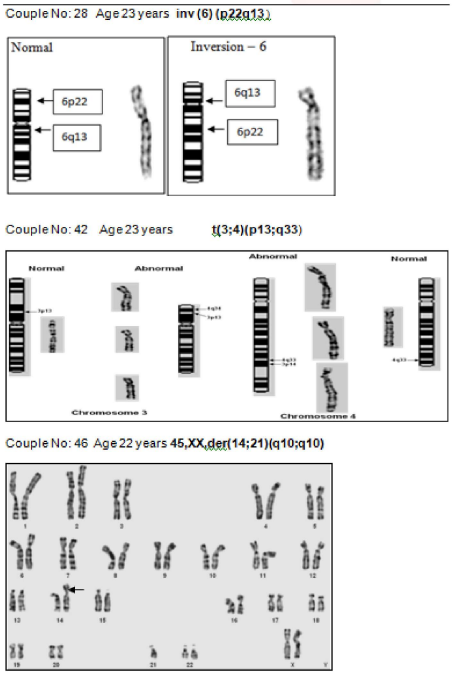


Fig. 2: Karyotypes Showing abnormal variations.

Fig. 3: Karyotype results of couples with BOH.

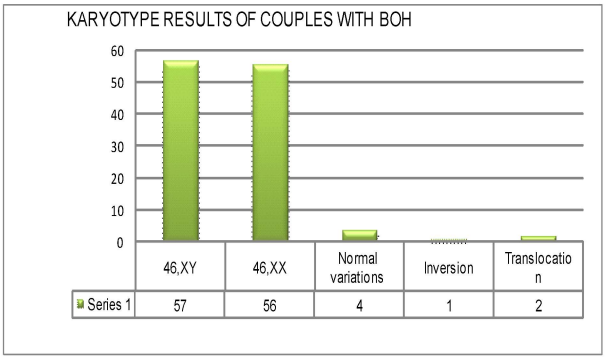
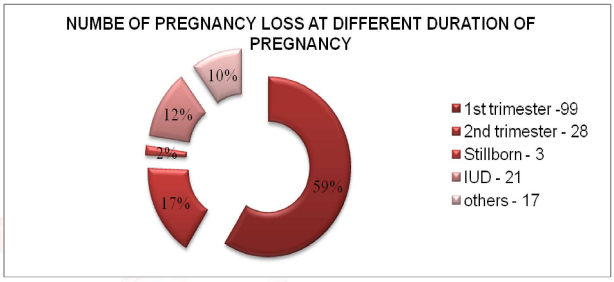


Fig. 4: Pregnancy loss at different duration of pregnancy.



Out of 60 couples 24 couples had the history of consanguineous marriage, among them 9 couples are of uncle niece relation, 13 couples are of 1st cousins and 2 couples are far relatives.

Table 1: Distribution of couples based on consanguinity.

	Relation	Number	Total	%
Consanguineous Marriage	Uncle niece	9[37.5%]	24	40
	1st cousins	13[54.16]		
	Far relative	2[8.33%]		
Non - consanguineous Marriage	----		36	60

Table 2: Cases with chromosomal abnormality, variations and outcome of their pregnancies.

Couple Number	Affected case	No: of pregnancies	Consanguinity	No: of anomalous pregnancy	No of Stillbirth IUD	No: of abortion in trimester		Karyotype
						1st	2nd	
14	Husband	3	+	2	0	0	2	46,XY,9qh+
20	Wife	4	-	0	0	3	1	46,XX,inv(9)(p11q13)
28	Wife	2	+	0	2	0	0	46,XX,inv(6)(p22q13)
41	Husband	2	-	0	0	2	0	46,XY,inv(9)(p11q13)
42	Wife	3	-	0	0	3	0	46,XX,t(3;4)(p13;q33)
42	Husband	3	-	0	0	3	0	46,XY,15p+
46	Wife	3	-	0	0	1	2	45,XX,der(14:21)(q10;q10)

DISCUSSION

Bad obstetric history implies previous unfavorable fetal out come in terms of 2 or more consecutive spontaneous abortions, early neonatal deaths, still births, intra uterine fetal death, intrauterine growth retardation and congenital

anomalies.

The karyotype analysis in couples with BOH helps to know the type of chromosomal abnormality associated with the couples and helps in providing proper genetic counseling about the probability of having future normal pregnancy, probability of having miscarriage or anomalous baby, about prenatal diagnosis and in vitro fertilization.

CA is included in the risk factors influencing the recurrence risk of pregnancy loss. Numerous studies have demonstrated that in around 5.5% of the couples, who have had RPL, one of the partners is the carrier for a balanced chromosomal rearrangement, in contrast to its incidence of less than 0.55% in the general population. It has been observed that the balanced chromosomal rearrangements have been detected to be present twice often in the female partners. In male the rearrangements are often associated with infertility [7].

The present study is based on karyotype analysis of 60 couples who presented with history of BOH.

Pregnancy loss at different duration of pregnancies: The study conducted by S.Dubey et al reports 78.3% of abortions were in the 1st trimester,20% in the 2nd trimester, 1.7% in the third trimester [8]. In the present study Out of 168 pregnancy losses 99 in 1st trimester, 28 in the second trimester, 24 in the third trimester, 17 others. In the study conducted by Warburton et al and Boue et al documented that chromosomal abnormalities account for at least 50% of all spontaneous losses and about 60% of first trimester losses [6].

Consanguinity and BOH: Most studies in India have shown that early postnatal mortality is higher in the progeny of consanguineous unions, due to expression of deleterious recessive gene. (10). Marriage is regarded as consanguineous if it has been contracted between spouses who are related as second cousins or closer, since the levels of homozygosity in marriages beyond second cousin differ only to a minor degree from those observed in the general population [10].

Study conducted by S Amudha et al reported 42.38% of couples with BOH had history of consanguineous marriage [11]. 46% of couples with BOH had history of consanguineous marriage in the study conducted by Razieh Dehghani Firoozabadi et.al [12]. In the present study Out of 60 couples 24 [40%] couples had the history of consanguineous marriage. Consanguinity may result in the homozygous condition for recessive autosomal/ deleterious genes. This homozygosity may have effect on the BOH. The incidence of consanguinity reported in India was 5-60% mainly of uncle niece and first cousin [13].

Incidence of chromosomal abnormalities: Numerous studies have shown that about 5.5% of couples experiencing three or more losses have one partner who carries a balanced chromosomal rearrangement, in comparison to less than 0.55% in general population. These rearrangements are detected twice as often in the female partners with history of pregnancy loss [2].

Razieh Dehghani Firoozabadi et al conducted study “cytogenetic analysis in couples with recurrent spontaneous abortion”. Karyotyping was performed on peripheral blood sample of 88 couples 11(12.5%) couples had abnormal karyotype [12]. Hemlata Purandare et al conducted Cytogenetic evaluation of 440 couples with BOH revealed chromosomal variations were observed in 7 individuals (3.5%) [14]. S.Dubey M.R et al conducted study on 742 couples with recurrent pregnancy loss, chromosomal abnormalities were found in 31[2%] [8]. In the present study out of 120 individuals [60 couples] 3 abnormal karyotypes were reported that is [2.5%]. In couples with bad obstetric history percentage of chromosomal rearrangement vary from 1-25% for individuals or 50% for couples the most frequently occurring chromosomal abnormality is chromosomal rearrangement that is translocation other chromosomal abnormalities see usually are sex chromosome mosaicism, inversion and ring chromosome. Reciprocal translocations are found to be 60% and Robertsonian translocation 40%. The Incidence of chromosoml abnormalities may differ between studies based on the their selection of the samples [15].

In a combined study done by collecting computerized database on 22,299 couples (44,398 individuals), 2.35% had CAs. Even from the pooled

data, statistically significant differences have not been observed between the major CAs and the types of reproductive wastage and / or the presence or absence of normal live births [16].

Karyotype results: Study results of Sayee Rajangam et.al.shows Chromosomal abnormality was found in 83 cases of the 1870 total samples (4.4%). The chromosomal variants were present in 79 out of the 1870 (4.2%). The structural chromosomal abnormality 49 (2.62%), The numerical abnormality in 34 (1.18%) [7].

Study results of S.Dubey M.R et al shows chromosomal abnormalities were found in 31[2%] individuals with 22(1.48%) structural and 9(0.6%) numerical abnormalities, 21[1.4%] were found to have chromosomal variants [8].

Study results conducted by Usha.R.Dutta et al 34(1.46%) show chromosomal abnormallities. 33[1.41%] cases showed structural aberrations, 1[0.04%] case of numerical anomaly. 44[1.89%] cases showed normal polymorphic variants [17].

Study conducted by Razieh Dehghani Firoozabadi et al revealed chromosomal abnormality in 9 (5.11%) couples. Numerical abnormality in 6(3.4%), structural abnormality in 3(1.7%), variation in 2(1.13%) [12].

In the present study 3 abnormal karyotypes were reported that is **[2.5%].** All 3 are structural abnormalities, 0 numerical abnormalities, 4(3.3%) chromosomal variation.

Table 3: Karyotype results in various studies.

Study	Chromosomal abnormality%	Structural abnormality%	Numerical abnormality%	Chromosomal variation%
Sayee Rajangam et.al. 2007 [7]	3.60%	2.62%	1.02%	4.20%
S.Dubey M.R et al 2007 [7]	2%	1.48%	0.60%	1.40%
Usha.R.Dutta et al 2011 [17]	1.46%	1.41%	0.04	1.89%
Dehghani Firoozabadi et al [3]	5.11%	1.70%	3.40%	1.13%
Present study	2.50%	2.50%	0	3.30%

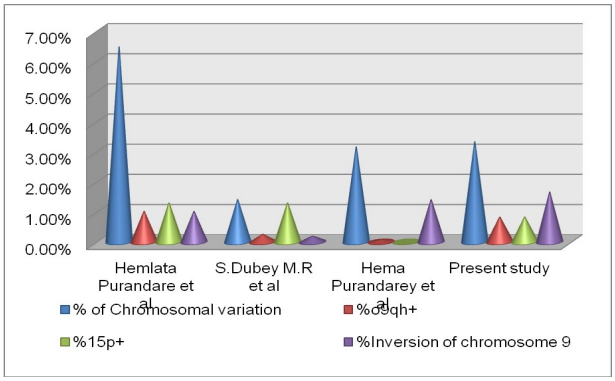
Fryns and Van Buggenhout reported that of the chromosome abnormalities observed in couples with two or more pregnancy loss, two third were balanced autosomal translocation, with incidence of such translocations being 30 times higher than the general population. Prospective studies on couples identified as balanced translocation carriers indicate that eighty percent of their pregnancies end in abortion, while sixteen percent lead to the birth of healthy new born;the risk of giving birth to an abnormal child with chromosome imbalance is approximately four to six percent. The specific chromosome involved in translocation also influences these statistics [2].

The risk of miscarriage in couples with reciprocal translocation is approximately 50% with Robertsonian translocation, the risk is approximately 25%. Most couples with balanced chromosome rearrangements have healthy children, however, homologous robertsonian translocation always result in fetal aneuploidy [18]. The carries of these translocations can exert negative effect on reproduction by producing an unbalanced gamets during meiotic segregation hence these carriers have an increased risk of abortions or child with an unbalanced karyotype compared to general population [7].

Chromosomal variations in couples withBOH: Study results of Hemlata Purandare et al chromosomal variations were observed in 57(6.47%) out of 880 individuals. 9qh+ seen in 9(1.02%) individuals 15p+ in 7(0.79%) individuals, inversion of chromosome 9 in 9(1.02%) individuals [14]. S.Dubey M.R et al conducted study on 742 couples with recurrent pregnancy loss 21(1.41%) cases with chromosomal variations were observed, 4 cases of 9qh+(0.26%), 3(0.2%), cases of pericentric inversion of chromosome – 9, 15p+ among 2(1.3%) cases.(8). Hema Purandarey et al conducted study observed 76(3.16%) cases of various chromosomal variation among 1200 couples, 34(1.41%) cases of inversion of chromosome – 9 , 2 cases of 9qh+(0.08%) [19].

In the present study out of 120 individuals 4(3.33%) cases showed chromosomal variation out of which 1(0.83%) case of 9qh+, 1(0.83%) case of 15p+, 2(1.66%) case of inversion of chromosome nine.

Fig. 5: Chromosomal variations in couples withBOH in various studies.



CONCLUSION

The present prospective study was done in 60 couples with Bad obstetric history in Division of cytogenetics, Department of Anatomy, Sri Siddhartha medical college.

The maximum number of pregnancy loss were found in 1st trimester. Incidence of consanguineous marriage is more among couples with bad obstetric history when compared to the general population.

Karyotyping helps in recognizing any chromosomal abnormality present in the couples with BOH with incidence of 2.4% in the present study, which may affect their future pregnancy.

Genetic counseling will be helpful in couples with chromosomal abnormality, about interventions in future pregnancies by knowing the cause for their recurrent pregnancy loss.

Larger studies is required to evaluate and understand the Other chromosomal abnormalities in couples with BOH responsible of causing pregnancy loss and congenital anomalies in the children.

ABBREVIATIONS

BOH- Bad Obstetric History
RM- Recurrent Miscarriage
OP- Out Patient
IP- In patient
PHA- Phyto haemagglutinin
CA- Chromosomal abnormality
RPL- Recurrent pregnancy loss
OBG- Obstetrics and Gynecology
RPMI medium- Roswell Park Memorial Institute medium
ISCN 1995- International System for Human cytogenetic Nomenclature
CCD- Charge couple device

ACKNOWLEDGEMENTS

I express my sincere thanks to Dr. Jayarama. S.Kadandale. Clinical cytogenetist, Department of anatomy, Sri Siddhartha Medical College, Tumkur who has always been encouraging and supportive. The production of this article would not have been possible without his kind help and guidance. I thankfully acknowledge the guidance and valuable suggestion of Dr Lakshmi Prabha Subhash , Professor And Head , Department Of Anatomy, Sri Siddhartha Medical College, Tumkur.

Conflicts of Interests: None

REFERENCES

[1]. Namrata Kumari, Norman Morris and Renu Dutta. Is screening of torch worthwhile in women with bad obstetric history : an observation from Eastern Nepal. J.Health Popul Nutr. 2011 Feb; 29(1):77-80.
[2]. David.L.Rimoin , J.Michael cannor, Reed.E.Pyeritz, Brucer.T.KORF. Emery and Rimons – Principles and Practice of Medical genetics .4th edition. Churchill Livingstone:Elsevier; 2007, p.845-61, 982-92.
[3]. Steven G Gabbe, Jennifer.R.Niebyl, Joe Leigh Simpson. Obstetrics normal and problem pregnancies. 5h edition. Churchill livingston an imprint of Elisvier . Piladelphia. Year; p.628-45.
[4]. Rema Devi, N Sreenivas, Sayee Rajangam. Bad obstetric History and Infectious causes. Int.J Hum Genet. 2002;2(4):269-271.
[5]. Dorthy Warburton, Jennie Kline, Zena Stein, Michelle Hutzler, Annie Chin, and Terry Hassold. Does the Karyotype of a spontaneous abortion predict the Karyotype of a Subsequent Abortion? – Evidence from 273 Women with Two Karyotyped Spontaneous Abortions. Am.J.Hum.Genet. 1987;41:465-83.
[6]. Ali Mohamad Malekasgar, Mohamad Esmaeil Motlagh, Mahmood Hashemi Tabar, Mohamad Ali Ghafari. Chromosomal analysis of couples with Bad Obstetric History. Iranian Journal of Pathology. 2006;1(3):91-98.
[7]. Sayee rajangam, Preetha Tilak, Arun N, Rema Devi. Karyotyping and counseling of bad obstetric history and infertility. Iranian Journal of Reproductive Medicine. 2007;5(1):7-12.
[8]. S Dubey, M.R.Chowdhury, B. Prahalad, V. Kumar, R. Mathur, Hamilton et al. Cytogenetic causes for recurrent abortion an experience of 742 couples [1484 cases]. Indian journal of humangenetics. 2005; 11(2):94-98.
[9]. Dorthy Warburton, Jennie Kline, Zena Stein, Michelle Hutzler, Annie Chin, and Terry Hassold. Does the Karyotype of a spontaneous abortion predict the Karyotype of a Subsequent Abortion? – Evidence from 273 Women with Two Karyotyped Spontaneous Abortions. Am.J.Hum.Genet. 1987;41:465-83.
[10]. A.H. Bittles. The impact of consanguinity on the Indian population. Indian journal of human genetics. 2002;8(2):45-51.
[11]. S.Amudh, N Aruna, S Rajanam. Consanguinity and Chromosomal abnormality. Indian Journal of Human Genetics. 2005;11(2):108-10.
[12]. Razieh Dehghani, Firoozabadi, Seyed Mehdi Klantar, Seyed Mohammad Seyed – Hasani, Nasrin Ghasemi et al. Cytogenetic analysis in couples with recurrent spontaneous abortion. Iranian Journal of Reproductive Medicine. 2006 May;4(1):13-17.
[13]. Kim HJ, Hsu LYF, Paciuc S, Cristian S, Quintana A,Hirschhorn K : Cytogenetics of fetal wastage. New England Journal of Medicine, 1975;293:844-847.

[14]. Hemalatha Purandare, Nandini Baz Fernandes, Sanjay Vasantrao Deshmukh and Sandesh Chavan. Heterochromatic Variations and Pregnancy Losses in Humans. Int J Hum Genet. 2011;11(3):167-75.

[15]. Babu V Rao, Lily Kerketta, Seema Korgaonkar, Kanjaksha Ghosh. Pericentric inversion of chromosome 9[inv(9)(912q13)]; its association with genetic diseases. Indian Journal of Human Genetics 2006 September;12(3):129-32.

[16]. De Braekeleer M, Dao TN. Cytogenetic studies in couples experiencing repeated pregnancy losses. *Hum Reprod* 1990;5:519-528.

[17]. Dutta U R, P Rajitha, P Vijaya Kumar and Ashwini B Dalal. Cytogenetic abnormalities in 1162 couples with recurrent miscarriages in Southern region of India: report and review. J. Assist Reprod Genet 2011;28:145-9.

[18]. D.K.James, P.J.steer, C.P.Weiner, B.Gonik. HIGH RISK PREGNANCY Management options. 3rd edition . Elsevier India private limited New Delhi; 2007.p.43-61,105-21.

[19]. Hema Purandarey, Prabodh Mallick, Vishalakshi Mamath, Sadhana Ghaisas. Prenatal Cytogenetic Diagnosis in Couples with Bad Obstetric History - A Study of 1200 Cases. Int J Hum Genet. 2006;(2):50-55.

How to cite this article:

Vidya H K, B S Suresh. CYTOGENETIC STUDY IN COUPLES WITH BAD OBSTETRIC HISTORY. Int J Anat Res 2017;5(4.3):4716-4722. DOI: 10.16965/ijar.2017.456