

PREGNANCY RATES AFTER COMPULSATORY ONE AND CONDITIONAL TWO EMBRIO TRANSFER POLICY

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SUMMARY

Objective: To predict our pregnancy rates after compulsory one and conditional two embryo transfer (ET) number.

Design: Retrospective Analysis.

Material and Methods: One or two embryos transferred 362 patient were analyzed between March 2010 and September 2011.

Results: Our clinical pregnancy rate was 31% and implantation rate was 25%. Our pregnancy rates after one or two ET were 30 and 32 % respectively ($P>0.05$). We transferred embryos at second, third day or blastocyst stage. Pregnancy rates were 19, 30 and 48 % respectively ($p< 0.001$), implantation rates were 14.5, 23.5 and 42.4 % respectively ($P< 0.001$). Our freezing rate was 39.5 %. From not to have freezing quality embryos to have, increased the pregnancy rate from 21% to %45 significantly. When one ET ed 95 % single and 5 % twins observed. When two embryos were transferred 81% single, 17% twin and 2 % triplets observed.

Conclusion: Pregnancy rates for one or two ET were statistically similar. If embryo quality allows us to culture up to blastocyst stage pregnancy rates were statistically increased. New Turkish ET policy resulted 95 % to 81 % single gestational sacs according to 1 or 2 ET at Gazi University IVF center.

Key words: SET, DET

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ZORUNLU TEK/ŞARTLI İKİ EMBRİYO TRANSFER YÖNETMELİĞİ SONRASI GEBELİK ORANLARIMIZ

ÖZET

Objektif: Gazi Üniversitesi Tıp Fakültesi, Kadın Hastalıkları ve Doğum Anabilim Dalı, Tüp Bebek Ünitesi zorunlu tek/şartlı iki embriyo transferi (ET) yönetmeliği sonrası gebelik hızlarımızın belirlenmesi.

Planlama: Retrospektif çalışma.

Hastalar: Merkezimizde Mart 2010 ve Eylül 2011 tarihleri arasında bir veya iki ET yapılan 362 hastanın sonuçları analiz edildi.

Değerlendirme parametreleri: Hastalarımızın ilk ultrasonları sonucu elde edilen verilere göre klinik gebelik, çoğul gebelik değerlendirmeleri yapıldı.

Sonuç: Merkezimizde yönetmelik sonrası klinik gebelik ve implantasyon oranımız % 31 ve 25'dir. Bir ve iki ET

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yapıldığında klinik gebelik oranlarımız % 30 ve 32' dir. ($P>0.05$). Merkezimizde ikinci, 3. gün ve blastosist ET klinik gebelik oranlarımız sırasıyla % 19, 30 ve 48 ($p< 0.001$) ve implantasyon oranlarımız % 14.5, 23.5 ve 42.4'dür. ($P< 0.001$). Dondurma hızımız %39.5 tur. Donduralacak kalitedede embriyosu olamamak/olabilmek gebelik hızını %21' den %45' e anlamlı arttırmaktadır. Bir ET yaptığımızda % 95 tekil ve % 5 ikiz gebelik ve 2 ET yaptığımızda ise % 81 tekil , %17 ikiz ve % 2 üçüz gebelik elde izlenmiştir.

Yorum: Bir veya iki ET sonucu klinik gebelik oranları istatiki olarak benzerdir. Embriyo kalitesi uygun olursa blastosist aşamasında ET yapabilmek gebelik oranlarını istatiki olarak arttırmaktadır. Yeni embriyo transfer politikası merkezimizde, bir/iki ET sonrasında gebelikler sirasi ile % 95 ve % 81 tek kesedir.

Anahtar kelimeler: SET, DET

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INTRODUCTION

"Regulations of Assisted Reproduction Treatment Applications and Assisted Reproduction Centers" which have published by law in Turkish Republic on 06.03.2010 have reduced the number of embryo transfers in IVF centers⁽¹⁾.

New regulation allows one embryo transfer in first and second treatment cycle and two embryos in third and more IVF cycles in women below 35 years old. Always allowed only two embryo transfer is in women 35 and over.

According to 2002 ESHRE consensus twin pregnancy is considered a complication and singleton pregnancy is suggested as normal⁽²⁾. In United States of America ASRM is suggested to limit number of transferred embryos as 1 or 2 in women below 35 years old⁽³⁾.

Multiple pregnancy may cause mother's death, congenital malformation and premature labor⁽⁴⁾. We evaluated clinical pregnancy results of Gazi University SOM IVF Center after new regulation for 1.5 years.

MATERIALS AND METHODS

This study includes clinical pregnancy results of Gazi University SOM IVF Center for 18 months between 06.03.2010 and 01.09.2011. Patients applied to our center were prospective cohort and evaluation criteria was age and the number of embryos that transferred. Detailed tables were formed to analyze statistically significant differences among data.

Chi square test and Epi Info were used to statistical evaluation. R value was calculated for linear regression to analyze two or more group data.

Results:

Three hundred sixty two of 465 IVF cycles which ended up oocyte pick-up and embryo transfer 77.8%. Clinical pregnancy and implantation outcome after transfer are 31% and 25% respectively (Table I).

Table I: Patient number, transferred patient number, clinic pregnancy rate and implantation rate.

Patient Number (n)	465/362
Clinic Pregnancy Rate (%)	% 31 (112/362)
Implantaion Rate (%)	% 25 (125/506)

After the new regulations of 2010, clinical pregnancy outcome of Gazi University SOM IVF Center is 30% as one embryo transfer and 32% as two embryo transfers. These statistics show that pregnancy outcome of one and two embryo transfers are similar statistically (Table II).

Table II: Embriyo Number and Clinic Pregnancy Rate ($*p>0.05$).

Embriyo Number (n)	Patient Number (n)	Clinic Pregnancy Rate (%)
1 *	216	%30 (65/216)
2 *	146	% 32 (47/146)

Age of 35 is a criteria of regulation. In our IVF center 41% of total transfers were at the age of 35 and above, whereas 59% of them were below. When we categorize patients as above 35 and below, clinical pregnancy rate in 1 embryo transfer is 25% whereas 36% in 2 embryo transfers the difference between these two groups was insignificant ($p=0.14$) (Table III).

Clinical pregnancy rate of patients below 35 with 1 embryo transfer is 31%, whereas 26% in 2 embryo transfer. One and two embryo transfer strategies give same pregnancy rate when stratified according to age Table III and IV.

Table III: Embriyo Number and Pregnancy (Over 35 Age) (* $p>0.05$).

Embriyo Number	Patient Number (n)	Clinic Pregnancy Rate (n)
1 *	% 37 (56/ 149)	%25 (14/56)
2 *	% 62 (93/ 149)	%36 (34/93)
Pregnancy Rate		%332 (48/149)

Table IV: Embriyo Number and Pregnancy (Below 35 Age) (* $p>0.05$).

Embriyo Number (n)	Patient Number(n)	Clinic Pregnancy Rate (%)
1 *	%76 (161/213)	%31 (50/161)
2 *	%24 (52 /213)	%26 (14/52)
Pregnancy Rate		%30 (64/213)

Pregnancy rate of patients with >35 and <35 ages are 25% and 31% in 1 embryo transferred cases whereas they are 36% and 26% in 2 embryo transferred cases respectively ($p=0.24$).

These results are statistically insignificant. In other words current regulations do not make a difference in pregnancy rate between patients below and above 35 years old (Table III and IV). Distribution of embryo transfers at the day of 2, 3 and blastocyst stage are 29%, 48% and 23% respectively. Clinical pregnancy rates according to the transfer day are shown in Table V. As it is shown in table, blastocyst transfer gives the highest pregnancy rates. Pregnancy rate elevation is statistically significant and linear. Implantation ratio is 25% for total population. As we consider implantation rates in respect to the transfer day, we see that transfers at the day of 2, 3 and at blastocyst stage have 14.5%, 23.5% and 42.4% implantation rates respectively ($p=0.001$), (Table VI). Increase of implantation rate of transfers at the day of 5 is statistically significant and linear. Freezing ratio of our IVF center is 39.5% (143/362). Although 3rd day transfer is frequently preferred in our center, freezing procedure is mainly applied in blastocyst stage. After transfer in cleavage stage, we incubate the rest of the embryos to the blastocyst stage and apply the freezing

protocol at this stage. Table VII shows the freezing days of the embryos.

Table V: Transfer Day (* $p>0.05$).

Transfer Day	Patient Number (n)	Clinic Pregnancy Rate (%)
2. Gün *	106 (% 29)	%19 (20 /106)
3. gün *	172 (% 48)	%30 (52/172)
Blastosist *	84 (% 23)	%48 (40/84)
Toplam	362	

Table VI: Transfer Day and Implantation Rate (* $p>0.05$).

Transfer day	Implantation Rate (%)
2. Day *	%14.5 (23/158)
3. Day *	%23.5 (57/242)
Blastocyt *	%42.4 (45/106)

Table VII: Freezing Day.

Freezing Day	
2. Day	% 8.3 (12/143)
3. Day	%38 (55/143)
5. Day	%38 (55/143)
6. Day	% 14.7 (21/143)
Total	143

When we consider the relationship between freezing or not and pregnancy rates we see that pregnancy rate is 45% in patients with freezing capability whereas it is 21% in patients whose embryos cannot be frozen. We see statistical reduction in pregnancy rates ($p=0.0001$). In other words new regulations improved the rates of pregnancy of patients which have embryos that can be frozen after transfer (Table VIII).

Table VIII: Freezing Rate and Pregnancy Rate.

	Patient Number % (n)	Patient Number (n) Freeze No	Total
Pregnancy positive % (n) *	%45 (65/143)	%21 (47/219)	112
Pregnancy negative % (n) *	%55 (78/143)	%79 (172/219)	250
			P<0.0001*

Table IX: Transfer Day, freezing Day and Pregnancy.

Transfer Day	Clinic Pregnancy Rate (%)	Clinic Pregnancy Rate (%)	Clinic Pregnancy Rate (%)	P-Value
	Overall Mean	Freeze Yes	Freeze No	
2. Day	%19 (20/106)	%33 (4/12)	%17 (16/94)	0.36
3. Day	%30 (52/172)	%42 (32/77)	%21 (20/95)	<0.02
Blastocyt	%48 (40/84)	%53 (29/54)	%37 (11/30)	<0.006
P-Value	0.001	0.07	0.26	

Preferring blastocyst stage transfer than cleavage stage transfer improved pregnancy rates of our center whereas it reduced the number of embryos which can be frozen. How is pregnancy rate is effected if there are enough blastocysts to freeze after blastocyst transfer?

Table IX shows that pregnancy rate is 19% whereas it is elevated to 33% in patient with freezable embryos. This increase is statistically insignificant.

Pregnancy rate of 3rd day transfer is elevated from 30% to 42% in patients who have freezable embryos after the transfer and this elevation is statistically significant. In blastocyst

stage transfer, pregnancy rate is elevated from 48% to 53% significantly. In other words patients who have freezable embryos after the blastocyst stage transfer have the highest pregnancy rate.

Transferred embryo counts and multiple pregnancy rates of our IVF center are shown in Table X. Pregnancy outcome after the new regulations are as the following: 89% singleton pregnancy, 10% in pregnancy and 1% triplet pregnancy. Ratios are like 95% singleton pregnancy and 5% twin pregnancy in one embryo transfer whereas they are 81% singleton, 17% twin and 2% triplet pregnancy in two embryo transfer. When we collect twin and triplet pregnancies of one and two embryo transfers pregnancy rate is elevated from 5% to 19% significantly.

Table X: Transfer and Pregnancy Rate (*p>0.05).

ET Number	Singleton	Twice*	Triplet*	Total N
				Number
1	%95 (61/64)	%5 (37/64)	0	64
2	%81 (39/48)	%17 (8/48)	%2 (1/48)	48
	%89 (100/112)	%10 (11/112)	%1 (1/112)	112

* Twice and triplet Pregnancy are shown as a multiple Pregnancy.

CONCLUSION

The randomized controlled study was performed by Gardner et.all which include ongoing pregnancy rate and implantation rate of 48 patient at 2004. The results was found 60.9% with transferred one blastocyt and 76% with transferred two blastosist⁽⁵⁾. There is no istatisticaldifferences between two groups like our study. But the Gardner's study is randomized controlled study but in our study transfer number was determined as a result of new legislation in Turkey. Another similar study which was done Veleva et all., there is no differences between pregnancy rates at SET and DET groups. Pregnany rates were given respectively 38.2 % and 33.1% (p=0.01)⁽⁶⁾.

At Clermont-Ferrand which transferred embriyo number determined like our legislation. Their pregnancies rates are 40.7% with one embriyo transferred patients who have least two good quality embriyo and 42.5 % with two embriyo transferred patients who haven't least two good quality embriyo⁽⁷⁾. These results are similar our results that embriyo transferred number determined independent of embriyo quality. Another study from the Medicana Fertilit Clinic, which seperate patients below and over 35 years , found pregnancy rate 34.5% which independent of age, 42.5 % under 35 years and 23.9 upper 35. Their twin rate is 5.3%. Our results are respectively, 31%, 30% and 32%. Our twin rate is 10%.

As a result of our study, patients under 35 years , who are transferred two embriyo dependent of legislation, are poor prognosis. Their pregnancy rate is 26%. Transferred one embriyo who are shown good prognosis pregnancy rate is 31 % . So under 35 years pregnancy rate similar. Patients, who are transferred two embriyo, have 35% pregnancy rate upper 35 years. Patients, who are transferred one embriyo, have 25% pregnancy rate as a result of poor prognosis. Pregnancy rate is found highest blastocyt transfers. Pregnancy rates are

increase with transfers are made respectively second day, third day and blastocyt transfers. Pregnancy rates are respectively 19,30, 48 %. Similar results are found at implantation rates. Implantation rates are respectively 14.5, 23.5, 42.4%. As a result embriyo transfers at blastocyt stage increase both pregnancy and implantation rates independent of transferred embriyo number. Previously studies were shown similar results (5,9,10).

If embriyo transfer at blastocyt stage ,pregnancy rate increase, also cryopreversation is done at the same cycle, pregnancy rate is found highest. After the new regulation, which main purpose of the new regulation has been reduce multiple pregnancies, our pregnancy outcome are 81% singleton, 17 % twin and 2 % triplet pregnancy. When we transfer two embriyo rather than one embriyo, our multiple pregnancy rate is elevated from 5% to 19%. Similar study, was done by Kalu et. all. Their results were 2.3% singleton pregnancy rate with one blastocyt transferred and 47.6% twin pregnancy rate with two blastocyt transferred which are like our results⁽¹¹⁾.

As a results ,transferred two embriyo rather than one embriyo has been still increase multiple pregnancy rate.

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