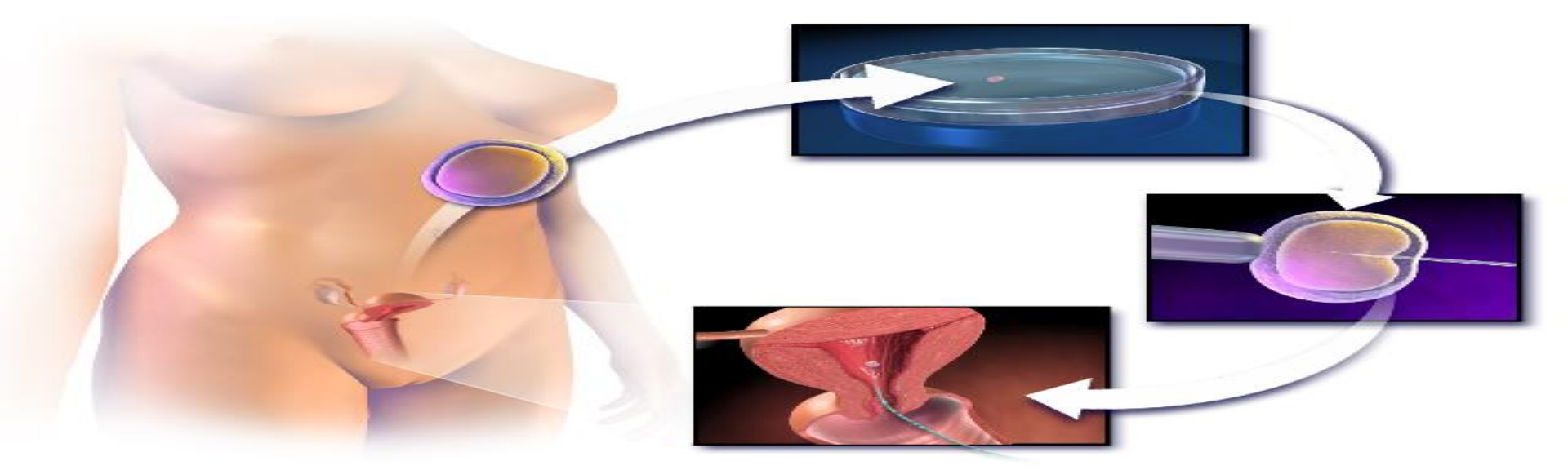


PREDICTIVE VALUE OF βHCG AFTER 14 DAYS OF EMBRYO TRANSFERATION

Nguyễn Xuân Hợi, MD, PhD

OVERVIEW

IVF - In Vitro Fertilization is a modern medical treatment for infertile couples with CPR about 40%.

After 14 days of embryo transferation, patients required βhCG blood test and transvaginal ultrasound at day 28th.

OVERVIEW

- ✓ Biochemical pregnancy: level of βhCG ≥ 5 mIU/mL and no embryonic sac via transvaginal ultrasound.
- ✓ Clinical pregnancy: image of embryonic sac via transvaginal ultrasound.

  In fact, level of βhCG after 14 days is relatively low. It caused anxious for both physicians and patients.

OVERVIEW

Objectives of our study is to determine the cut-off of βhCG at day 14th after embryo transferation in order to prognose outcome of IVF treatment.

ROLE OF BETA HCG TO PREGNANCY

- hCG (Human Chorionic Gadonatropin) secreted by placenta, its presence in maternal blood and urine, and used as a biomarker for pregnancy.
- hCG help retaining luteal phase.
- Level of βhCG increasing rapidly after conception make itself an important marker for early detection and monitoring pregnancy.

ROLE OF BETA HCG TO PREGNANCY

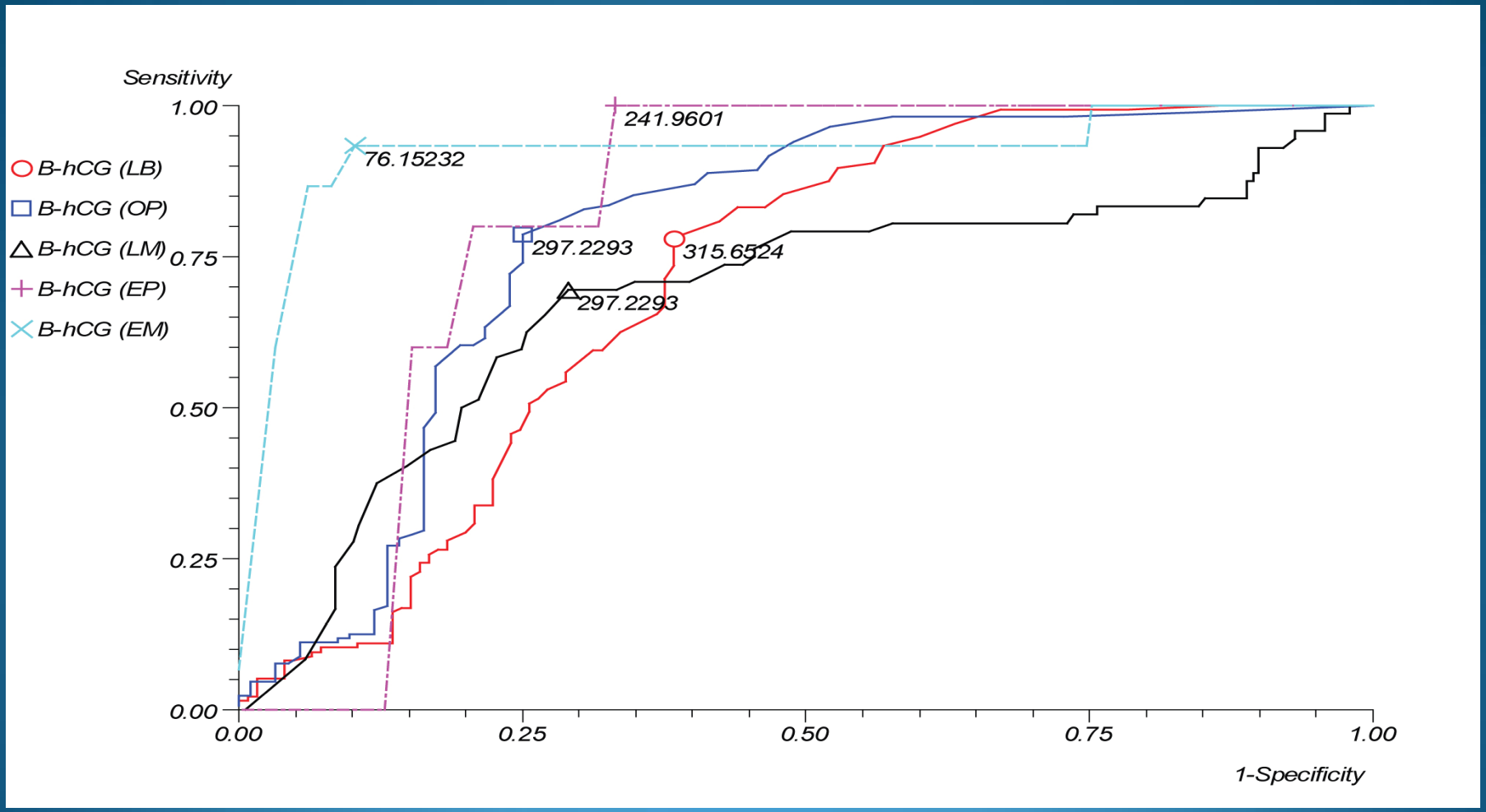
- Level of βhCG lower in IUGR and ectopic pregnancy.
- Level of βhCG higher in multiple pregnancy and molar pregnancy.
- Peak of hCG in maternal blood is at 8 to 10 week of gestation. From 10 week of gestation to late pregnancy, hCG is secreted by placenta to maintain and sustain the development of fetus. From that point, level of hCG is not increasing and no longer exist in maternal blood after 4 week of delivery.

STUDY ON βhCG AND OUTCOME OF IVF

Research of Mamdoh A.Eskandar (2011): follow-up 261 ICSI/IVF cycles positive with hCG after 14 days of embryo transferation.

	Cut - off	Area Under ROC	Sensitivity	Specificity
Live – birth	315.65	58.14%	77.94%	61.60%
Ongoing pregnancy	297.23	62.92%	78.70%	75.00%
Late miscarriage	297.23	67.72%	69.44%	70.90%
Ectopic pregnancy	241.96	81.17%	100.00%	66.80%
Early micarriage	76.15	91.19%	93.33%	89.84%

STUDY ON βhCG AND OUTCOME OF IVF



Mamdoh A.Eskandar, 2011.

STUDY ON βhCG AND OUTCOME OF IVF

Research of P.Poikkeus (2002): study on 774 IVF cycles with βhCG ≥ 5 IU/L after 12 days of ET (IVF: 518, ICSI: 119, FET: 137)

- Mean of βhCG level in viable pregnancies including singleton, twin and triplet is 126 IU/L, and in non-viable pregnancies including biochemical, ectopic pregnancy 31 IU/L.
- Mean of βhCG level in twin doubled compare to singleton (201 IU/L vs 115 IU/L).

STUDY ON βhCG AND OUTCOME OF IVF

hCG concentrations (IU/mL) in viable and non-viable pregnancies

	n	%	Median	Range
Viable pregnancies	459	59.1	126	5 - 683
• Singletons	362	47	115	5 - 397
• Twins	96	12	201	48 - 683
• Triplets	1	0.1	317	317
Non-viable pregnancies	315	40.9	31	5 - 268
• Biochemical	154	20	18	5 - 81
• Ectopic	20	3	35	5 - 144
• Miscarriages, all	138	17.6	60	5 - 268
• Miscarriages, late	5	0.6	96	74 - 116
• Hydatidiform mole	2	0.3	99	39 - 160
Total	774	100		

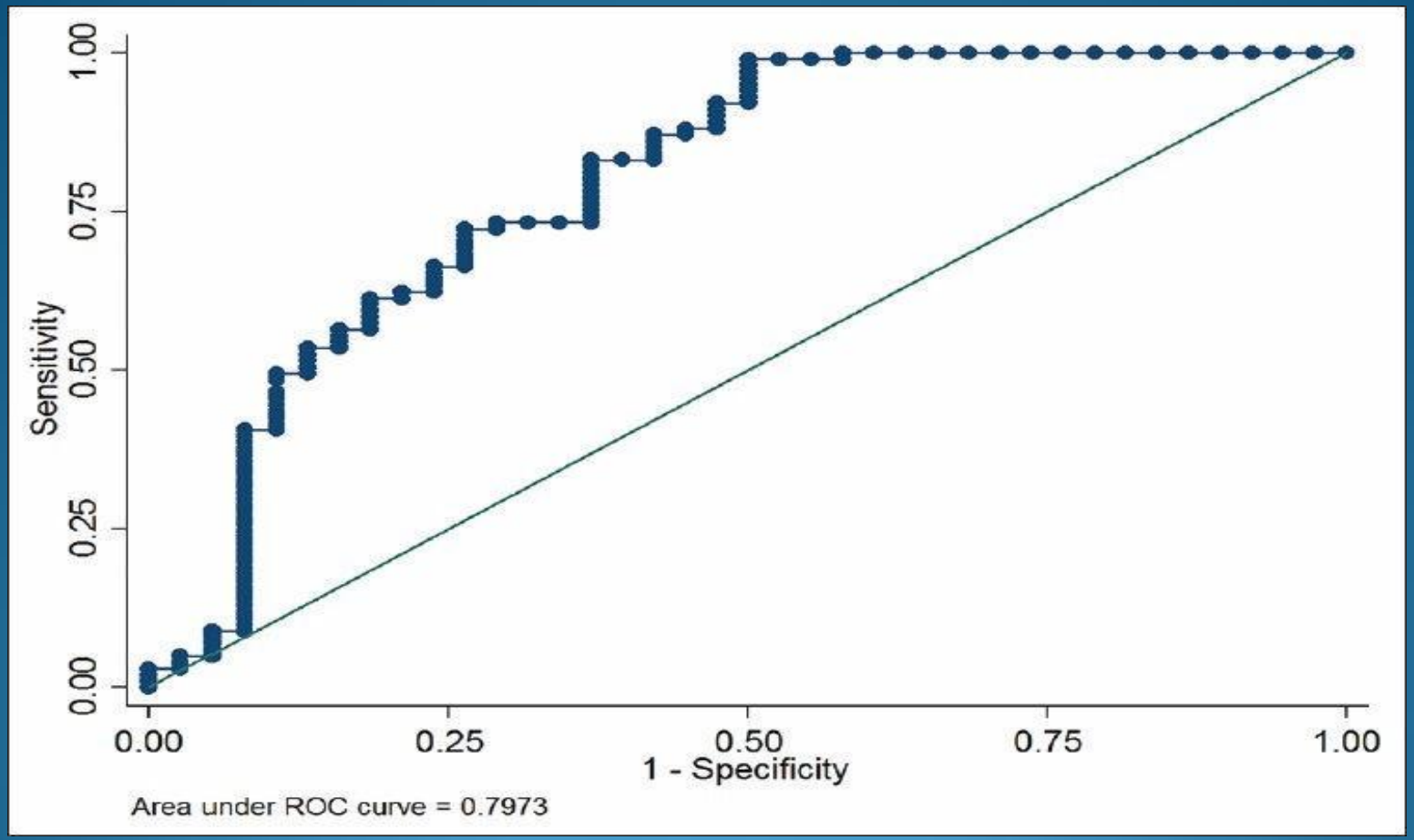
P.Poikkeus, 2002

STUDY ON βhCG AND OUTCOME OF IVF

Neeta Singh, et al 2013 studied on 171 IVF cycles with βhCG after 14 days of ET: mean of βhCG level in viable pregnancies is 625 mIU/mL, in non-viable pregnancies is 174 mIU/mL.

Cut-off point of βhCG in prognosis of 12 week of gestation was 347 mIU/mL with 72,2% sensitivity and 73,6% specificity, AUC = 0,79.

STUDY ON βhCG AND OUTCOME OF IVF



Neeta Singh et al, (2013)

STUDY ON βhCG AND OUTCOME OF IVF

- Xiao-yan HUANG, et al (2007) studied on 384 pregnancy after IVF with βhCG test after 11 days of ET: βhCG level from 10 to 50 mIU/mL, PPV for biochemical and ectopic pregnancy is 81,8%, NPV was 94,4%.
- Maysa M.Khadra (2016) studied on 248 IVF cycles with βhCG level after 14 days of ET in viable pregnancies is 264 mIU/mL, in non-viable pregnancies is 120 mIU/mL.

Objectives and methodology

- This is a retrospective study in 1228 IVF cycles in Center for Assisted Reproduction, NHOG from 2014 to 2015, with βhCG blood test 14 days after ET ≥ 5 mIU/mL.
- Exclusion criteria: hCG injection after ET, ET in other center, inadequate information.

RESULTS AND DISCUSSION

Mean of βhCG level between clinical and biochemical pregnancy

βhCG / Fetal state	n	X SD	p
Clinical preg.	1080	761,5 706,33	0,001
Biochemical preg.	148	161,02 82,35	

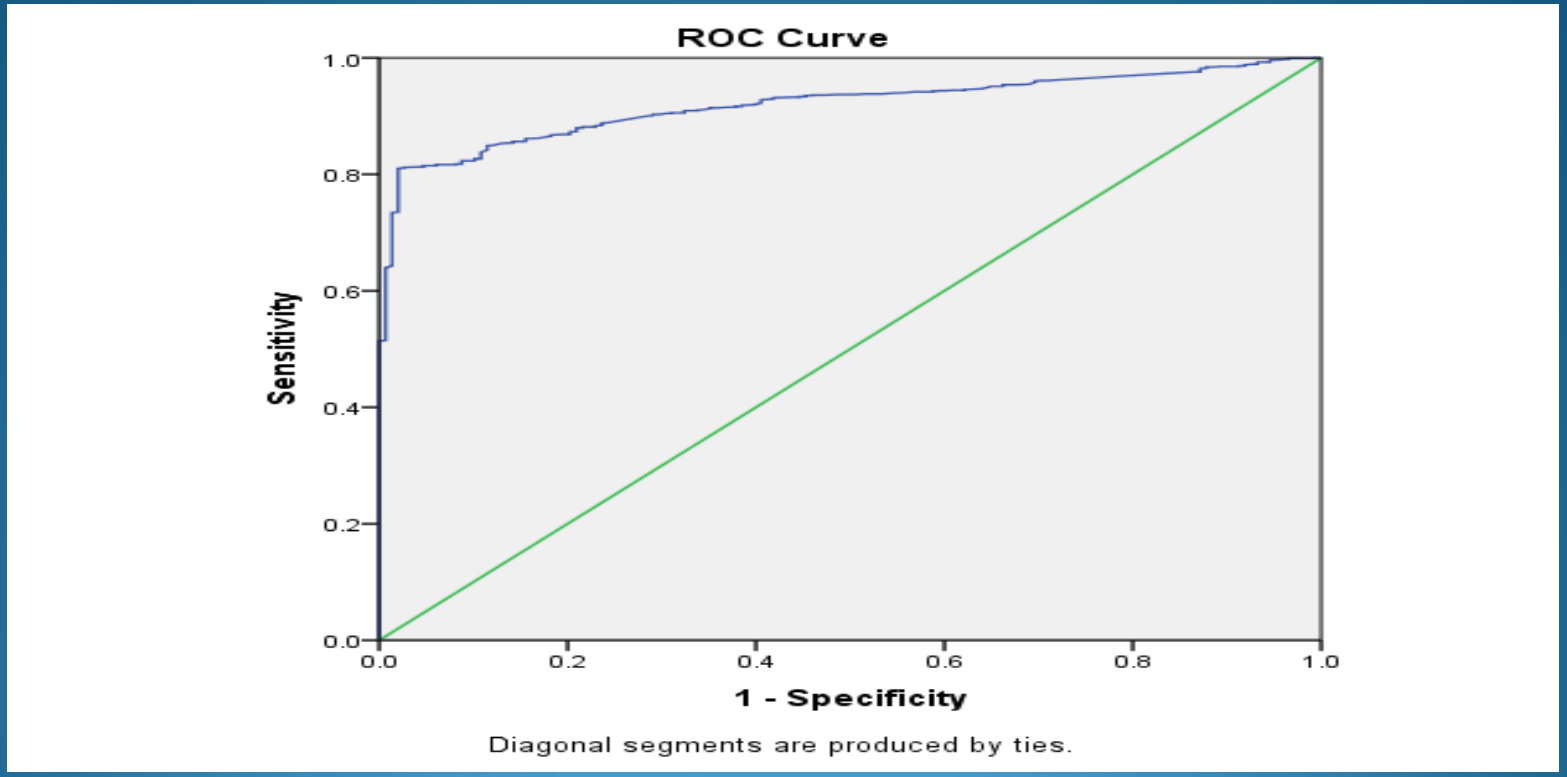
RESULTS AND DISCUSSION

Predictive value of βhCG with clinical preg.

Value / βhCG (mIU/mL)	Sen %	Spec %	J value
291	81,5	95,3	0,768
293,5	81,4	95,3	0,767
294,5	81,3	95,3	0,766
296	81,2	97,3	0,785
298	81,1	97,3	0,784
299,5	**81,0**	**98,0**	**0,79**
300,5	79,3	98,0	0,773
301,5	79,2	98,0	0,772
303	78,9	98,0	0,769
304,5	78,6	98,0	0,766
307	78,3	98,0	0,763

RESULTS AND DISCUSSION

ROC curve of βhCG in clinical preg.



AUC = 0,919, p < 0,001 and 95% CI (0,9-0,94).

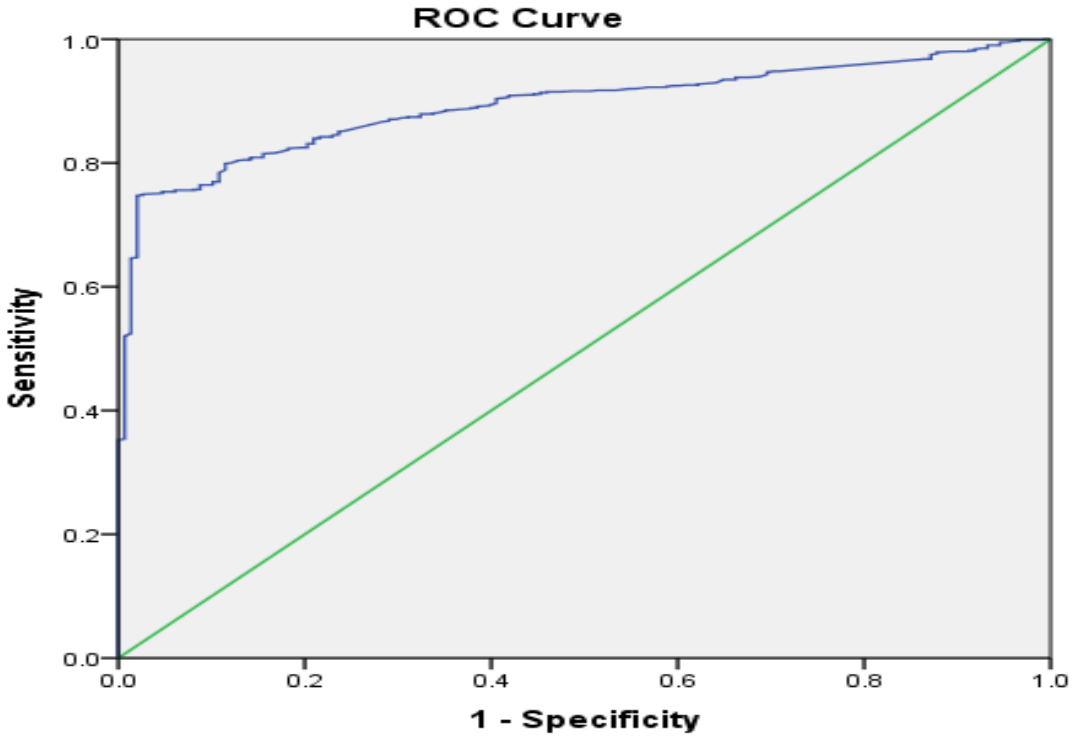
RESULTS AND DISCUSSION

Predictive value of βhCG with biochemical preg.

value / βhCG (mIU/mL)	Sen %	Spec %	J value
109,5	76,0	93,1	0,691
111	76,5	93,1	0,696
112	76,2	93,5	0,697
114,5	76,0	94,1	0,701
114,5	76,0	94,1	0,701
115,5	**76,0**	**95,0**	**0,71**
116,5	75,7	95,0	0,707
117,5	75,2	95,0	0,702
117,5	75,2	95,0	0,702
118,5	74,1	94,5	0,686
120	73,4	94,5	0.679

RESULTS AND DISCUSSION

ROC curve of βhCG in biochemical preg.



AUC = 0,893, p < 0,001 and 95% CI (0,87-0,92).

RESULTS AND DISCUSSION

Relation between number of transfered embryos and multiple pregnancy

Number of fetus / Number of embryoes		Singleton	Multiple Preg.	Total	P
1	n	24	0	24	0,001
	%	3,9%	0%	2,2%	
2	n	49	19	68	
	%	8,0%	4,1%	6,3%	
3	n	425	356	781	
	%	69,8%	75,9%	72,4%	
4	n	111	94	205	
	%	18,2%	20,0%	19,0%	
Total	n	609	469	1078	
	%	100%	100%	100%	

RESULTS AND DISCUSSION

Relation between number of transfered embryos and multiple pregnancy

- The rate of multiple pregnancy is directly proportional to the number of transfered embryoes.
- The rate of multiple pregnancy in 3 embryoes transfered group (75,9%) is significantly higher than that of 2 embryoes (4,1%), $p < 0,001$.
- In the same group, the rate of multiple pregnancy is higher than singleton (75,9% vs 69,8% in 3 embryoes transfer), (20% vs 18,2% in 4 embryoes transfer).

RESULTS AND DISCUSSION

Relation between number of embryonic sac and mean of βhCG

Embryonic sac	n	%	Mean of βhCG X SD (mIU/mL)	P
1	609	56,5	581,86 670,22	
2	358	33,2	934,01 663,99	
3	105	9,7	1211,21 779,69	0,001
4	6	0,6	1069,27 646,01	
Total	1078	100%		

RESULTS AND DISCUSSION

Relation between number of embryonic sac and mean of βhCG

- Mean of βhCG in single embryonic sac is 581,86 670,22 mIU/mL, 934,01 663,99 mIU/mL in 2 embryonic sacs, 1211,21 779,69 in 3 embryonic sacs, 1069,27 646,01 mIU/mL in 4 embryonic sacs.
- Mean of βhCG in multiple pregnancy is significantly higher than singleton, $p < 0,001$.

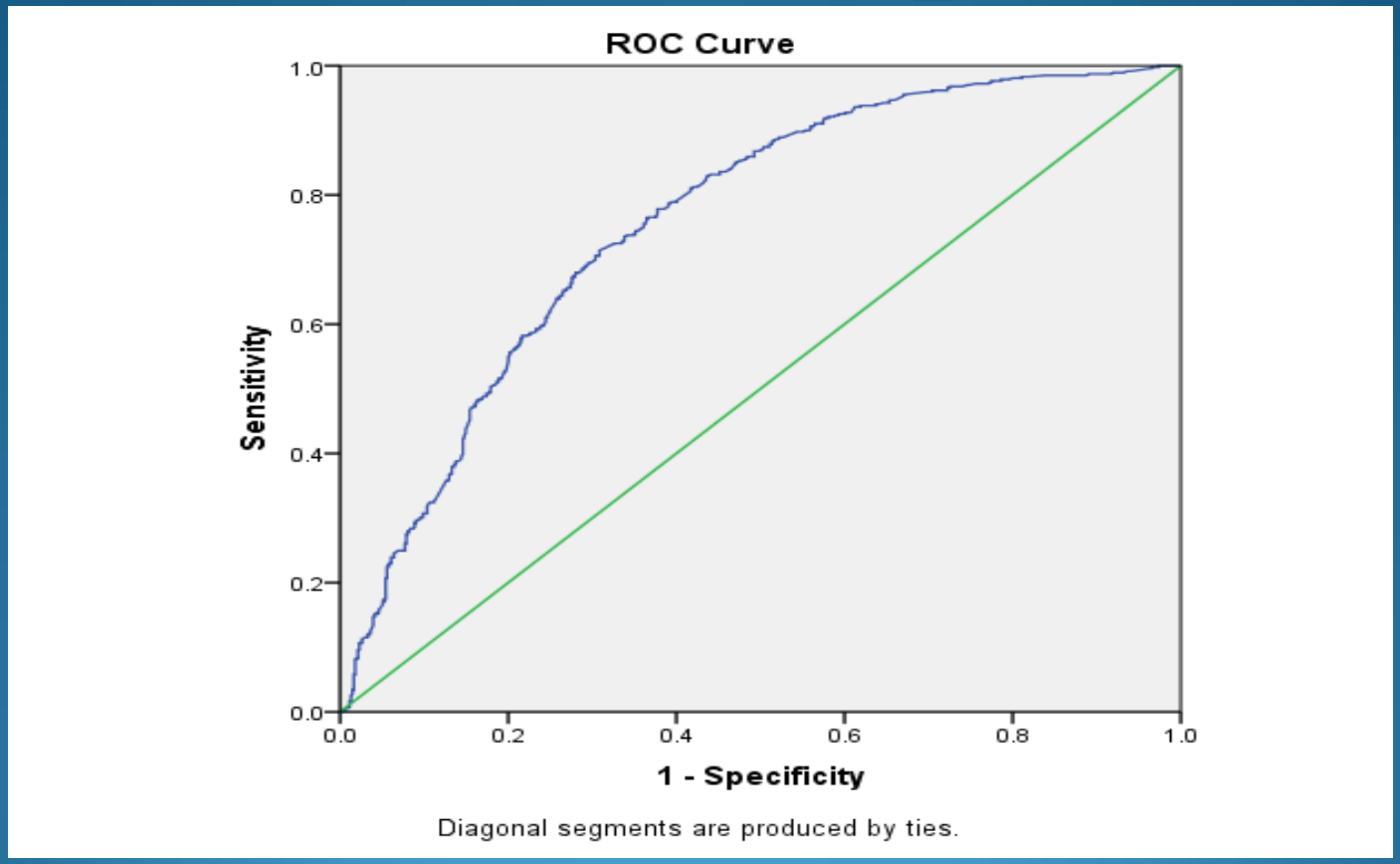
RESULTS AND DISCUSSION

Predictive value of βhCG to fetal conditions

βhCG(mIU/mL)	Sen %	Spec %	J value
592,0	72,7	66,3	0,39
594,5	72,7	66,5	0,392
597,0	72,5	66,5	0,390
598,5	72,5	67,0	0,395
599,5	72,5	67,3	0,398
600,5	**71,4**	**69,1**	**0,405**
601,5	71,0	69,1	0,401
602,5	70,8	69,1	0,399
603,5	70,6	69,1	0,397
604,5	70,6	69,3	0,399
606,0	70,6	69,5	0,41

RESULTS AND DISCUSSION

βhCG ROC curve in prognosis of multiple pregnancy



AUC = 0,759, p < 0,001, 95% CI (0,73 – 0,79).

CONCLUSION

- Mean of β-hCG level at 14 days after ET in clinical pregnancy is 761,5 706,33 mIU/mL and biochemical pregnancy is 161,02 82,35 mIU/mL.
- Mean of βhCG in single embryonic sac is 581,86 670,22 mIU/mL, 934,01 663,99 mIU/mL in 2 embryonic sacs, 1211,21 779,69 in 3 embryonic sacs.
- The rate of multiple pregnancy is directly proportional to the number of transfered embryoes.
- Cut-off of βhCG for prognosis of multiple pregnancy is 600,5 mIU/mL, with 71,4% Sen, and 69,1% Spec.
- βhCG cut-off after 14 days ET for clinical pregnancy is 299,5 mIU/mL with 81% Sensitivity and 98% Specificity; for biochemical pregnancy is 115,5 mIU/mL with 76% Sensitivity and 95% Specificity.
- Level of βhCG 14 days after ET is valuable in prognosis outcome of pregnancy.


Thank you for your attention!