

HUMAN CHORIONIC GONADOTROPIN (hCG)

INTRODUCTION

Human chorionic gonadotropin (HCG) is a glycoprotein that consists of 2 subunits (alpha and beta) which are associated to comprise the intact hormone. Unique biochemical and immunological properties of HCG are due to beta subunit. HCG is produced by placenta during pregnancy; it serves to maintain the corpus luteum during pregnancy and also influences steroid production. It is also used as tumor marker for Choriocarcinoma and some Germ cell tumors. Alpha subunit is usually associated with Lung cancer & Pancreatic islet cell cancer.

NORMAL RANGE

<5 mIU/mL

CLINICAL USE & LABORATORY DIAGNOSIS

1. Diagnosis of pregnancy
2. Detection of ectopic pregnancy
3. Gestational Trophoblastic Disease
4. Germ Cell Tumors
5. Prenatal screening

I) Diagnosis of pregnancy

HCG in mIU/mL	Status of Pregnancy
<5	Negative
5-25	Indeterminate
>25	Positive

Normal pregnancy

HCG IN mIU/mL	Post conception
5	8-11 days
25	First day of missed period
Doubles in 1.5 days	2-5 weeks
Doubles in 2-3 days	>5 weeks
100,000	8-10 weeks

Presence of twins approximately doubles HCG concentration.

II) Detection of ectopic pregnancy

- Slow increase in HCG (<66% in 48 hours during first 40 days of pregnancy) indicates Ectopic pregnancy in 75% of cases.

- Levels of 1500-2000 mIU/mL with no gestation sac in TVS
- Levels of 6500 mIU/mL with no gestational sac in USG
- Rising or similar HCG levels post curettage indicate Ectopic pregnancy
- Initial serum HCG levels are the single best prognostic indicator of successful treatment with single dose methotrexate

III) HCG in Gestational Trophoblastic Disease

- Comprise Molar and Non molar placental tumors.
- Risk factors include:
 - Advanced maternal age
 - Asian ethnicity,
 - Low socioeconomic status
 - Previous molar pregnancy
 - Higher HCG levels

Non molar placental tumors (Gestational Trophoblastic Neoplasia)

Placental tumors that aggressively invade into the myometrium & metastasize. Diagnosed by persistently elevated HCG levels.

Criteria for diagnosis

- Plateauing levels (+10%) for days 1,7,14, 21 over 3 weeks
- Rise of serum HCG levels >10% during three weekly consecutive measurements
- Serum HCG levels remains detectable for 6 months or more
- Histological criteria for Choriocarcinoma

Molar pregnancy (Hydatidiform Mole)

Following evacuation:

- Obtain baseline HCG levels
- Repeat HCG test every 1-2 weeks;
- Usually negative by 40 days (75%)
- Positive at 56 days (50% possibility of trophoblastic disease)
- Rising or plateauing levels demand evaluation for trophoblastic disease
- HCG levels >500,000 mIU/mL - diagnostic of invasive mole.
- Once normal - monthly followup for 6 months and then discontinue

IV) Germ Cell Tumors

Along with AFP useful in classifying Germ Cell Tumors–

- Seminoma
- Yolk sac Tumor
- Embryonal carcinoma
- Teratoma.

Germ cell tumor type	AFP	HCG
Seminoma	Not elevated	Elevated in 10-30% cases
Yolk sac tumor	Elevated	Not elevated
Choriocarcinoma	Not elevated	Elevated
Embryonal Carcinoma	Elevated	Elevated
Teratoma	Not elevated	Not elevated

- In 90% patients with **Non-Seminomatous tumors** one or both markers along with LDH may be affected correlating with:
 - ✓ tumor volume and
 - ✓ disease prognosis
 - ✓ Disease recurrence
 - ✓ Development of metastasis

Stage of disease	Percentage population affected
Stage I	<20
Stage II	50-80
Stage III	90-100

V) HCG in Prenatal Screening

To identify women for increased risk of fetal abnormalities between 15-20 weeks of gestation when used in conjunction with AFP, Free estriol (Triple marker) & InhibinA (Quadruple marker).

HCG levels	Possible Abnormality
Increased Average MoM of 2.06	Down Syndrome (70% detection)
Reduced	Trisomy 18
<ul style="list-style-type: none"> • Unexplained elevation with MoM from 2 to >4– Rule out : <ul style="list-style-type: none"> • Fetal chromosomal abnormalities, • Molar pregnancy, • Multiple pregnancy, 	Association with Perinatal complications <ul style="list-style-type: none"> • IUGR • Gestational hypertension with proteinuria

<ul style="list-style-type: none">• Fetal demise,• Chorioangioma of the placenta	<ul style="list-style-type: none">• Preterm labour / delivery
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INTERPRETATION

Increased Levels

- Non seminomatous germ cell testicular tumors (40-50%)
- Seminoma (20-40%)
- Ovarian Germ cell tumors – Dysgerminoma, Yolk sac tumor, Immature teratoma, Mixed germ cell tumor, embryonic carcinoma
- Gestational Trophoblastic disease
- Non germ cell tumors – Melanoma & Carcinomas of breast, GI Tract, Lung & Ovary
- Benign conditions like Cirrhosis, Duodenal ulcer and Inflammatory bowel disease

LIMITATIONS

- This test is not recommended to screen Germ cell tumors in the general population.
- False negative / positive results are observed in patients receiving mouse monoclonal antibodies for diagnosis or therapy
- HCG levels may appear consistently elevated / depressed due to the interference by heterophilic antibodies, nonspecific protein binding, HCG like substances & certain medications