MODELLING THE POTENTIAL EFFECTIVENESS OF DIFFERENT SCREENING AND TREATMENT STRATEGIES FOR HEPATITIS C DURING PREGNANCY IN EGYPT

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Introduction

- HCV-RNA prevalence among Egyptian pregnant women was estimated to be 2.4% in 2013[1]
- Meta-analysis of the risk of vertical HCV infection to children of HCV antibody–positive and RNA-positive women was about 5.8%[2]
- HCV screening is not systematic during pregnancy
- Pregnant and breastfeeding women are one of the few population subgroups that are not eligible for DAA treatment

We aimed to explore the potential impact of different HCV screening and treatment strategies during pregnancy in terms of:

- Maternal cure
- Vertical transmission (VT)

Method

Study design: Decision analytic Markov model to simulate the trajectory of hypothetical cohort of yearly pregnant women in Egypt according to five different HCV screening and treatment strategies (Table 1)

Input parameters: Uptake of screening/treatment, prevalence of HCV and VT risk factors[3-5] , and pregnancy events[5-8], were based on data from the literature and key assumptions (Table 2). Probabilities of VT (defined as having at least 2 PCR positive or antibody-positive lasting over 18 month or a single PCR positive + antibody positive when last seen) were based on estimates from a Bayesian model using data from three European cohorts.

Table 1: Strategies

	Screening	Treating
S0	Current standard of care with limited risk-based screening targeting women with planned caesarean-section	No treatment
S1	S0+optimal screening of all women with HCV risk factors* (adapted who recommendation)	
S2	S1+optimal screening of HIV-positive women	DAA treatment† in pregnancy for HCV-positive women with VT risk factors**
S3	Optimal screening of all pregnant women	
S4	Optimal screening of all pregnant women	DAA treatment† in pregnancy for all HCV-positive women

*HCV risk factors: screening in presence of jaundice, surgery, liver disease, transfusion with blood or other blood components, needle-stick injury with a contaminated needle, tattoos, endoscopy, renal dialysis, dental care or tooth extraction, drug injection or other medications using shared needles (adapted to the Egyptian context from WHO recommendations); †DAA treatment is assumed to start from 7th month of pregnancy; **VT risk factors once screened: presence of HIV infection and/or high HCV viral load>6 log-IU/ml,

Table 2: Data on the proportion of screened individuals according to each strategy

	Uptake of screening strategies				Uptake of treatment†
	Absence of HCV risk factor*		At least one HCV risk factor*		
	HIV-positive	HIV-negative	HIV-positive	HIV-negative	
S0	30% when planned caesarean-section, 5% otherwise		60% when planned caesarean-section, 30% otherwise		0%
S1	30% when planned caesarean-section, 10% otherwise		80%	80%	0%
S2	80%	30% when planned caesarean-section, 10% otherwise	80%	80%	70% of those with VT risk factor**
S3	80%	80%	80%	80%	70% of those with VT risk factor**
S4	80%	80%	80%	80%	70% of all HCV+ women

*HCV risk factors: screening in presence of jaundice, surgery, liver disease, transfusion with blood or other blood components, needle-stick injury with a contaminated needle, tattoos, endoscopy, renal dialysis, dental care or tooth extraction, drug injection or other medications using shared needles (adapted to the Egyptian context from WHO recommendations); †DAA treatment is assumed to start from 7th month of pregnancy; **VT risk factors once screened: presence of HIV infection and/or high HCV viral load>6 log-IU/ml,

Sensitivity analysis: We performed one-way sensitivity analysis varying values of input parameters that may change our results:

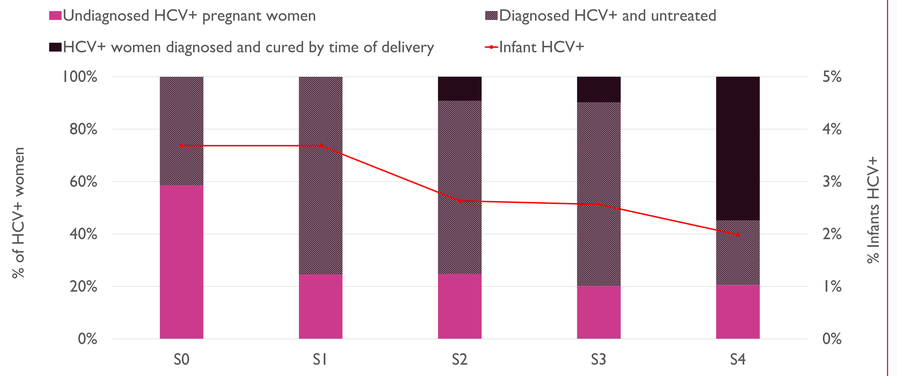
First, in baseline analysis, we assumed that all HIV infected women were unaware of their infection and not treated: to be conservative we changed this parameter to 16% of aware-suppressed HIV women which is consistent with Unicef data[9]. Based in this same data, we changed the uptake of screening in S2 among HCVRF-, HIV- from 80% to 16% when non programmed C-section delivery. Furthermore, given the uncertainty in the literature on the proportion of individuals having high viral load among HCV positive, we also considered a higher proportion of 86% (vs 18%) cited in Italian data[10]

Results

Baseline analysis

- When considering screening targeting pregnant women having programmed C-section (S0), a total of 66,290 HCV-positive women would transmit HCV infection to 2 440 new-borns (3.7%) during one year
- Screening according to WHO recommendations (S1) would detect 76% of HCV-positive women compared to 41% with (S0)
- DAA treatment in pregnancy for HCV-positive women with VT risk factors would result in 9-10% cured pregnant women at the end of pregnancy depending on screening strategy (risk based screening in S2 vs universal screening in S3) and decrease VT to 2.6%
- Universal screening and treatment of all pregnant women would result in the highest proportion of women diagnosed and achieving HCV cure by delivery (54%) and the lowest number of children with VT (2%)

Figure 1: Proportions of HCV-positive (HCV+) women undiagnosed, diagnosed but untreated, or cured by time of delivery, and infants with HCV infection (among the population of initially HCV+ pregnant women) according to each strategy (Tables 1 & 2).



	S0	S1	S2	S3	S4
Number (%) of still HCV+ women at delivery	66,270 (100%)	66,270 (100%)	60,140 (91%)	59,820 (90%)	30,590 (46%)
Undiagnosed HCV+ pregnant women	38,820 (59%)	15,940 (24%)	15,940 (24%)	13,290 (20%)	13,290 (20%)
Diagnosed HCV+ pregnant women but not treated	27,450 (41%)	50,330 (76%)	43,980 (66%)	46,290 (70%)	16,000 (24%)
Cured women after DAA	-	-	6,130 (9%)	6,450 (10%)	35,680 (54%)
HVC+ infants	2,440 (3.7%)	2,440 (3.7%)	1,730 (2.6%)	1,690 (2.6%)	1,300 (2.0%)

Sensitivity analysis:

- When we decreased the screening uptake in S2 and when we increased the proportion of HIV suppressed women, the results remain unchanged.
- By contrast, when we varied the proportion of women with high viral load (from 18% to 86%), VT is threefold higher (11.6% vs 3.7% in S0 baseline analysis); however, S2 and S3 (strategies with targeted treatment to high risk of transmission women) are more effective in curing mother (44% and 46% vs 9-10% in baseline analysis).

Discussion

- Current screening and treatment strategy is associated with the highest rate of VT (3.7%)
- Our estimates are in line with published results, even if lower that the pooled estimate of VT risk reported in the meta-analysis of Benova et al[2], i.e. 5.8% among HIV negative pregnant women, showing a high level of heterogeneity: maternal HIV status, definition of HCV infection, age of child at HCV infection determination, selection of women, and loss to follow-up being independently associated with variation in the risk of VT
- The model does not take into account spontaneous HCV clearance in children that may have underestimated VT.
- During sensitivity analysis, varying the uptake of screening in S2 and/or the proportion of HIV treated and suppressed coinfected women did not change our results; this may be explain by the low HIV prevalence
- By contrast, higher HCV viral load significantly increased VT. HIV coinfection has been found to be associated with high viral load[11]. However, HIV coinfection being low in Egypt, the higher HCV viral load found in Italy may not be pertinent in Egypt
- Universal screening and treatment would achieve optimal outcomes but our model does not take into account costs

Conclusion

- This is one of the first models to explore the potential benefits of HCV screening and treatment strategies in pregnancy, which will be critical in informing future care and policy as more safety/efficacy data emerge.
- This model demonstrates that universal HCV screening and treatment during pregnancy is effective.

References

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