

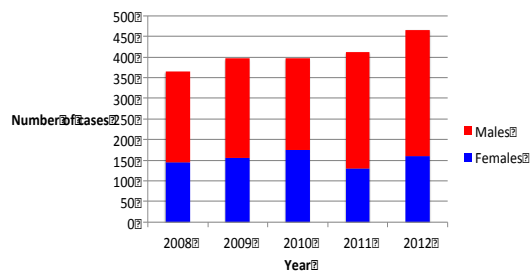
The consideration of sex and gender in diagnosis and management of blood-borne viruses: the case of hepatitis C

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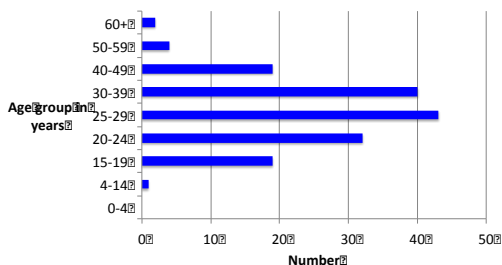


New cases of HCV in Australia, 2008-2012



Source: National Notifiable Diseases Surveillance System

New cases of HCV in Australian women, 2012



Source: National Notifiable Diseases Surveillance System

Women, oestrogen and disease progression

- Antifibrinogenic effect of oestrogen on the liver (Shimizu et al 1999 & Di Martino et al 2004)
- Faster disease progression in women linked to menopause and observed changes in hormone levels according to reproductive status (Villa et al 2012)
- Hormone replacement therapy has been shown to slow the progress of liver fibrosis in menopausal women (Di Martino, Lebray et al. 2004) and is associated with a lower risk of Hepatocellular Carcinoma (Yu, Chang et al. 2003)

Women, oestrogen and treatment

- Women of childbearing age have higher rates of sustained virologic response, but current therapies are contraindicated during pregnancy
- Older women are more likely to develop fibrosis and are less responsive than younger women to pegylated interferon and ribavirin (Villa et al 2010)
 - Higher baseline levels of liver inflammation, fibrosis, steatosis, serum interleukin-6, and hepatic TNF- α among postmenopausal women than women of reproductive age
 - Early menopause \downarrow treatment response
- Higher oestrogen states are hypothesized to promote sustained virologic response

Investigating long-term opiate use and oestrogen

- Opioid-induced hypogonadism (diminished functional activity of the gonads that may result in diminished sex hormone biosynthesis) (Confrancesco, Shah et al 2006; Abs, Verhelst et al 2000; Daniell 2004)
- Hypogonadism associated with:
 - decreased libido
 - tiredness
 - depressed mood
 - hot flashes or night sweats
 - Infertility
 - osteoporosis and fractures
 - abnormal menses in women
 - inhibition of oestradiol and adrenal androgen production
- Bone density testing and HRT may be appropriate therapy



Heroin, methadone and oestrogen

- Methadone and hypogonadism link in men (Hallinan, Byrne et al 2008; Rubinstein, Carpenter et al 2013)
- Assess the association between opiate substitution therapy and levels of sex hormones in women with HCV
- Observational study to assess the impact of long-term (≥ 2 years) methadone use on sex hormone levels in women with HCV
- Blood samples were taken two weeks apart to measure sex hormones (oestradiol, progesterone and follicle stimulating hormone (FSH))



Results

- 8 (40%) showed evidence of a disrupted menstrual cycle with possible effects on fertility status, for which opioid use may be a contributory factor.
 - Six (33%) had normal oestrogen but undetectable progesterone at both visits (possible non-ovulation)
 - Two (10%) were oestrogen deficient (hypogonadotrophic hypogonadism)
- Compared to 4.6% women in larger population study (Munster et al 1992).



Feasibility of the study

- Successful despite barriers to collecting blood in this population
- Exclusions
 - 9 lost to follow-up (not able to attend 2nd visit)
 - 1 excluded as breastfeeding
 - 1 excluded as not currently on OST (methadone)
 - 1 excluded as on OCP (the pill)
- Participants were interested
- Participants were pleased to receive a copy of their pathology results
- Support from peer user organisations



Participant characteristics

- 20 pre-menopausal women
- Mean age 34.9 years (range 21 - 46 years)
- Methadone prescribed and 17 (85%) had used heroin in the past 12 months
- Amenorrhea or an irregular menstrual cycle reported by 9 (45%)



Results - hypogonadism

	Participant 1	Participant 2
Age	41 years old	29 years old
Opioid use	Methadone (13 years) and regular heroin use (once a week - 5 times per week, ~20 years)	Methadone (14 months) and regular heroin use (daily, ~15 years)
BMI	20.31	20.32
Menstruation	Irregular periods	Regular periods
Fecundity	Three children, one miscarriage	One child, multiple miscarriages
Fractures	Toe fracture	No fractures
HCV diagnosis	1994	2003



Why is this important?

- Further evidence and discussion of the implications of HCV in women who use opioids
 - HCV progression
 - bone mineral density
 - fertility
- More information is needed to bring this information into clinical practice
 - hormone replacement therapy (HRT)
 - hormonal contraception



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