

**DDW 2007:
Top Ten Posters**
by Alan Franciscus

DDW was an interesting conference this year because most of the new information on various topics, including drugs in development, disease progression, epidemiology, and current treatments were already presented at EASL (European Association for the Study of Liver Disease) in April 2007. However, there were many new posters on HCV-related topics that were not covered by the press, as well as other studies that were covered by the press but which warranted additional mention. Listed below (in no particular order) are the top ten posters that I covered while at DDW. (*Alan Franciscus*)

(Since there is a shortage of available livers more liver transplant centers are using livers that are not typically used in liver transplantation. The two posters below are good examples of efforts to use 'less than perfect' livers for transplantation.)

2. Use of hepatitis C-infected donors in liver transplantation: a case-control study

P. Kwo; S. Wilson; R. S. Mangus; A. Tector; J. A. Fridell; R. Vianna; S. Liangpunsakul; V. Misra; S. Bhardwaj

Background:

Hepatitis C is the major reason for the increase in HCC (Liver Cancer) the need for liver transplantation in the United States. To meet the increasing demand for cadaveric donor livers (from deceased donors), some centers transplant livers from hepatitis C (HCV)-infected donors into recipients with HCV-related cirrhosis. This study utilizes a case-control design to compare transplant outcomes for 38 recipients of livers from HCV-infected donors to those for 76 standard, non-extended criteria (ECD) donors (1 case / 2 controls) between 2001–2006.

Methods

Data was extracted from the transplant center registry, UNOS (United Network for Organ Sharing) data, and from the original on-site donor data chart. Thirty percent of all donors met non-ECD criteria (standard donors) and were included as potential matches for the case-control study. Each HCV-positive liver donor recipient was matched to two standard donor recipients as matched standard donor controls (MSDC) by:

- recipient age +/- 10 years,
- primary diagnosis,
- cancer stage for those with HCC,
- recipient MELD +/- 5, and
- donor age +/- 10 years.

Outcomes included graft and patient survival at 3-months, 1-year and 2-years; perioperative death; and, HCV recurrence by 4-month and 1-year fibrosis (F0-F4-Metavir).

Results

The HCV-donor and matched standard donor control groups did not differ for recipient or donor demographics or in cold and warm ischemia (decrease in the blood supply) time. Survival results and fibrosis progression are shown in the table. Median follow-up time was 36 months. Kaplan-Meier actuarial survival demonstrated improved graft survival for HCV-infected donors with a trend toward significance ($p=0.10$).

Conclusions

These preliminary results suggest that HCV-infected liver transplant recipients receiving livers from HCV-infected donors may have a slower rate of fibrosis progression at 1-year. A trend was seen in survival advantage for those receiving HCV-donor grafts compared to standard donor controls. The use of HCV positive donors may be considered as a first line therapy to increase the available donor pool of organs in those undergoing liver transplantation for HCV-related cirrhosis.

Survival analysis for hepatitis C-infected liver transplant recipients for donors previously infected with hepatitis C (n=38) or matched standard donor controls (n=76)

| | Hepatitis C-Infected Donor | Matched Standard Donor Controls (MSDC) | p-value |
|---|----------------------------|--|-------------|
| TOTAL | N=38 | N=76 | |
| 90-Day Survival | | | |
| Graft | 37/38 (97.4%) | 72/76 (94.7%) | NS |
| Patient | 37/38 (97.4%) | 72/76 (94.7%) | NS |
| 1-Year Survival | | | |
| Graft | 30/31 (96.8%) | 62/72 (86.1%) | NS |
| Patient | 31/31 (96.8%) | 63/72 (87.5%) | NS |
| 2-Year Survival | | | |
| Graft | 16/19 (84.2%) | 49/62 (79.0%) | NS |
| Patient | 17/19 (84.2%) | 52/62 (83.9%) | NS |
| Graft Loss within 7 Days | 1/38 (2.6%) | 1/76 (1.3%) | NS |
| Mean Fibrosis at 4 Months (F0-F4) | 0.68 | 0.33 | 0.08 |
| Mean Fibrosis at 12 Months (F0-F4) | 0.86 | 1.05 | NS |
| Percent Change in Fibrosis | 26% | 69% | |

S1736. Impact of Extended Criteria Donor Livers on Survival of Patients with Hepatocellular Carcinoma.

A. Cooper; R. S. Mangus; M. Maluccio; R. Vianna; J. A. Fridell; A. Tector.

Introduction/Aim:

Liver transplantation is the most effective treatment for patients with hepatocellular carcinoma (HCC), with optimal outcomes in those meeting Milan criteria. With a growing shortage of donor livers, patients outside Milan criteria are rarely transplanted, though these patients have improved survival with transplantation. Extended criteria donor (ECD) organs are increasingly utilized to meet the demand for transplant livers. The purpose of this study is to evaluate the impact of ECD livers on post-transplant survival in patients with HCC, both inside and outside Milan criteria.

Methods:

Records from 698 consecutive adult liver transplants from July 2001 to June 2006 were reviewed. Of these patients, 138 (19.8%) had HCC and 489 (70%) received ECD livers.

Primary ECD criteria included: age ≥ 60 , BMI ≥ 35 , maximum AST or ALT > 500 , maximum bilirubin > 2.0 , peak serum sodium > 170 , HBV/HCV/HTLV reactive, non-heart beating donor, cold ischemia time > 12 hours, ICU stay > 5 days, ≥ 3 pressors simultaneously, and extensive chronic alcohol abuse.

Outcomes included 1- and 2-year survival and HCC recurrence. Kaplan-Meier estimates of survival time for ECD vs. standard donor (SD) groups were compared using the log-rank test. The simultaneous impact of MELD score, primary

diagnosis, recipient age, transplant year and Milan status for patients in the two groups was evaluated by a Cox proportional hazards model.

Results:

Median follow-up for the entire population was 25.4 months from the date of transplantation. Median follow-up for survivors was 31.8 months.

Of the 138 patients, 31 (22.5%) have died: 10 (7%) died of cancer, 4 (3%) died of recurrent hepatitis C and liver failure, 7(5%) died of other or unknown causes. There are 107 (77.5%) patients who are currently alive, 6 (4.3%) with and 101 (73.2%) without evidence of disease recurrence. No patients were lost to follow-up.

The estimated mean survival from the date of transplant was 52.4 months for patients in the DS group and 54.8 months in patients receiving ECD (p=0.61 by unpaired t-test with Welch's correction). Overall actuarial survival at 1 year was 85% (ECD 83.6%, SD 87.5%), and 77% at 2-years (ECD 77.3%, SD 76.9%).

Discussion:

The use of extended criteria donor livers increases organ availability for patients with liver disease and provides acceptable survival in patients with HCC. In this cohort of patients transplanted with HCC, there was not significant difference in overall survival between those receiving a standard donor liver and those receiving an ECD liver. Additionally, tumor recurrence rates did not differ between the ECD and SD groups. Thus, transplantation with ECD livers does not appear to impart any oncologic detriment for patients with HCC. These results suggest that ECD

livers represent a viable avenue for expanding the opportunity to offer transplant to patients with CCC, even those who are not typically considered acceptable candidates.

Conclusion:

There was no difference between the ECD and SD groups in tumor recurrence. Overall survival was also the same regardless of Milan criteria. These results suggest that ECD livers represent a viable avenue for expanding the opportunity to offer transplant to patients with HCC, even those who are not typically considered acceptable candidates.

(The information on the two drugs discussed below was also presented at EASL but I have highlighted it because of the encouraging results.)

442. Phase II Study of celgosivir in combination with Peginterferon alfa-2b and ribavirin in chronic hepatitis C genotype-1 non-responder patients

K. D. Kaita; E. M. Yoshida; D. Kunimoto; F. Anderson; M. Sherman; P. Marotta; L. J. Scully; K. M. Peltekian; R. A. Enns; F. Diaz-Mitoma; S. S. Lee; L. Worobetz; J. Pankovich; A. Petersen

Introduction:

Celgosivir is a new class of antiviral medicine (glucosidase I inhibitor) in clinical development for the treatment of chronic hepatitis C virus (HCV) infection. Researchers tested this new antiviral medicine and measured its potential to offer improved treatment outcomes when combined with other anti-HCV drugs.

Methods:

The current study evaluated 57 chronic HCV genotype-1 patients, separated by prior treatment status into non-responders or partial responders and randomized to three treatment groups:

1. Celgosivir 400 mg once daily in combination with peginterferon alfa-2b and ribavirin (**PRC**);
2. Celgosivir 400 mg once daily in combination with peginterferon alfa-2b (**PC**); or
3. Placebo with peginterferon alfa-2b and ribavirin (**PR**, active control).

All patients were treated for 12 weeks. The non-responders cohort enrolled 36 patients (**PRC**: 15 pts; **PC**: 11 pts; **PR**: 10 pts) and the partial responder cohort had 21 patients (**PRC**: 3 pts ; **PC**: 9 pts; **PR**: 9 pts).

Results:

For prior non-responder patients, an Early Viral Response (EVR) was achieved in 42 percent (5/12) of those in which celgosivir was added to the standard peginterferon alfa-2b and ribavirin therapy compared with only 10 percent (1/10) of patients receiving just peginterferon alfa-2b and ribavirin.

Non-responder patient study results also demonstrate an improved mean decrease in HCV viral loads when celgosivir is added to peginterferon alfa-2b and ribavirin of $1.63 \log^{10}$ IU/mL versus $0.92 \log^{10}$ IU/mL in patients treated with peginterferon alfa-2b and ribavirin alone. Eleven of the 36 non-responder patients were classified as a very difficult-to-treat patient subgroup (null responders) as they were shown to

have a prior HCV treatment response of $\approx 0.4 \log^{10}$ to optimized therapy. In the present study, the mean decrease in HCV viral loads in these null responder patients was $1.86 \log^{10}$ IU/mL with celgosivir plus peginterferon alfa-2b and ribavirin while the two null responder patients treated with peginterferon alfa-2b and ribavirin was $0.32 \log^{10}$ IU/mL. The observed difference in mean viral load between the PRC and PR treatment groups provides evidence that the combined effect of celgosivir with peginterferon alfa-2b and ribavirin provides a clinically significant treatment benefit for difficult-to-treat chronic HCV infected patients.

Conclusion:

"This study is the first demonstration that celgosivir in combination with peginterferon alfa-2b and ribavirin results in a clinically significant decrease in HCV viral loads in patients highly resistant to current standard treatment," said Kelly D. Kaita, M.D., of the University of Manitoba in Canada, and lead author of this study. "Further clinical research on the best dosing regimen and combinations is warranted to optimize the potential of this innovative combination for chronic HCV patients."

Source: DDW press release

T1044. Eltrombopag Maintains Platelet Counts During Myelosuppressive Pegylated Interferon Alpha Treatment of Chronic Hepatitis C Virus Infection.

G. M. Dusheiko; J. G. McHutchison; N. H. Afdhal; M. L. Shiffman; M. Rodriguez-Torres; S. Sigal; M. Bourliere; T. Berg; N. Blackman; F. M. Campbell; S. White.

Background/Aims:

Eltrombopag is an oral, non-peptide, small molecule thrombopoietin receptor (TPO-R) agonist. The safety, efficacy and pharmacokinetics of eltrombopag in



HCV-infected subjects with thrombocytopenia (low platelets) precluding initiation of pegylated-interferon (PEG-IFN) and ribavirin have previously been reported. We have now examined the ability of eltrombopag to counteract the myelosuppressive effects of pegylated-interferon on platelet counts in HCV-infected patients during treatment. A sub-analysis of data from study TPL102357 was performed to determine if eltrombopag is able to maintain platelet counts in thrombocytopenic subjects during pegylated-interferon treatment thus avoiding deleterious dose reductions of pegylated-interferon.

Methods

HCV positive subjects with compensated cirrhosis and platelet counts 20-70,000/uL were randomized (1:1:1:1) to receive 30mg (10 pts), 50mg (14 pts), 75mg (21 pts) eltrombopag or placebo once daily for 4 weeks (induction phase).

Subjects achieving platelet counts of $> 70,000/uL$ in the induction phase could initiate pegylated-interferon plus ribavirin therapy along with study drug for 12 weeks (maintenance phase). Platelet count assessments made at the baseline visit were compared to those made at the completion of study drug concomitant with pegylated-interferon plus ribavirin (Study Day 113).

Results/Conclusion

A total of 74 subjects were enrolled and 49 of those successfully initiated pegylated-interferon plus ribavirin.

- Eltrombopag effectively maintained platelet counts above 50,000/uL in up to 81% of patients during the first 12 weeks of antiviral treatment, counteracting the myelosuppressive effects of pegylated-interferon.

- Eltrombopag use avoided the need for pegylated-interferon dose modification in approximately 90% of patients during the first 12 weeks of antiviral treatment.
- Further research into the long-term use (48 weeks) of eltrombopag in patients with HCV –associated thrombocytopenia is warranted.

(The durability of a sustained virological response reported in this large clinical trial on continued SVR 5 years post treatment is certainly hopeful information for those people who achieve SVR and those people who are contemplating treatment.)

444. Sustained Virologic Response (SVR) Resulting From Treatment with Peginterferon Alfa-2a (40KD) (PEGASYS®) Alone or in Combination with Ribavirin (COPEGUS®) is Durable and Constitutes a Cure: an Ongoing 5-year Follow-up.

M. G. Swain; M. Lai; M. L. Shiffman; W. E. Cooksley; A. Abergel; A. Lin; E. Connell; M. Diago

Background:

The current standard of care in chronic hepatitis C virus (HCV) infection is combination therapy with peginterferon and ribavirin. Sustained virologic response (SVR) rates of up to 66% have been reported in patients with HCV mono-infection. The durability of SVR is being investigated in a long-term follow-up study of patients treated for chronic HCV infection. Here we present the latest results of this ongoing study.

Methods:

Patients who took part in one of nine randomized trials of peginterferon alfa-2a (40KD) (PEGASYS®) as monotherapy or in combination with ribavirin (COPEGUS®), and who were negative for serum HCV-RNA (<50IU/mL) at the

final virologic assessment were eligible for inclusion in the long-term follow-up study. Serum HCV-RNA was determined annually for 5 years from the date of last treatment.

Results:

To date 997 patients are undergoing long-term follow-up, including 163 HCV mono-infected patients treated with peginterferon alfa-2a (40KD) monotherapy, 741 mono-infected patients treated with combination therapy, and 93 HIV-HCV co-infected patients treated with either monotherapy or combination therapy. The overwhelming majority of patients (989/997; >99%) remain HCV-RNA negative at a mean of 4.1 (range 0.4-7) years after treatment cessation (an outcome that the authors consider to be consistent with a cure).

Eight patients became HCV-RNA positive (>50IU/mL) between 1.1-2.9 (mean 2.0) years after completing treatment. There were no consistent patterns in terms of age, gender or HCV genotype among these 8 patients and none showed evidence of liver cirrhosis. Two patients had low baseline viral load (<400,000IU/mL) while the remaining 6 patients had a baseline viral load ranging from 700,000–12 million IU/mL. The proportion of these incidents representing new infections or true ‘relapse’ is currently unknown.

Conclusions:

- These results show that an SVR following treatment with peginterferon alfa-2a alone or in combination with ribavirin is durable in almost all (99.2%) patients with chronic HCV infection, validating the use of the word ‘clinically cured’ for those achieving an SVR.

- The author noted that of the 8 patients who became HCV positive during follow-up, that one was a clear case of reinfection because that patient tested positive for a different genotype than the genotype in the original study.
- The authors are not sure if the other 7 patients are from reinfection or because the virus returned after therapy. Another physician from the audience suggested that because there is a 1% false-positive the viral load was a false positive. Unfortunately, those patients have been lost to follow-up.

| Treatment (population) | Number of studies | N | Mean years after treatment | Patients with detectable HCV RNA (n) |
|---|-------------------|-----|----------------------------|--------------------------------------|
| Monotherapy (elevated ALT) ^a | 4 | 163 | 4.6 | 2 |
| Combination (elevated ALT) ^a | 4 | 666 | 4.2 | 5 |
| Combination ('normal' ALT) | 1 | 75 | 3.2 | 0 |
| Mono and combination (HIV-HCV co-infection) | 1 | 93 | 3.2 | 1 |

^a1 study contained monotherapy and combination therapy arms.

(The study below is disconcerting because the majority of patients reported that their doctors did not offer HAV vaccination. This poster speaks to the need for more education of providers and patients to help get populations at risk for HAV vaccinated to prevent even more damage to the liver.)

M1002. Barriers to Vaccination against Hepatitis A among Patients Coinfected with HIV and Hepatitis C.

S. Dhalla; C. T. Tenner; N. E. Shukla; A. Aytaman; G. Villanueva; G. Punla; C. Patterson; J. Comas; E. J. Bini

Background:

Hepatitis A virus (HAV) superinfection is associated with a high risk of mortality in patients with chronic liver disease. HAV vaccination is recommended for all



patients with chronic hepatitis C virus (HCV) infection, as well as for those with HIV infection. Although patients with HIV/HCV have a dual indication for HAV vaccination, it is unknown how many of these individuals receive the vaccine in clinical practice. We hypothesized that HIV/HCV coinfecting patients would be more likely to receive the HAV vaccine than those with HIV or HCV monoinfection.

Methods:

Patients with known HIV and HCV status completed a detailed questionnaire at the time of their scheduled visit to the outpatient primary care or gastroenterology clinic at 3 study sites. Data collected included patient demographics, personal vaccination history, and barriers to vaccination.

Results:

Among the 2,038 patients, 715 were uninfected, 121 had HIV, 893 had HCV, and 309 had HIV-HCV.

Overall, 360 of the 2,038 patients (17.7%) were told by their doctor that they had been exposed to HAV, including 4.2% of the uninfected patients, 15.7% of those with HIV, 23.2% of those with HCV, and 33.7% of the coinfecting subjects ($P < 0.001$).

Among the 1,650 patients who were not previously exposed to HAV, only 412 (25.0%) reported that they received the vaccine, 900 (54.5%) were not vaccinated, and 338 (20.5%) did not know if they were vaccinated.

The proportion of patients vaccinated against HAV differed significantly according to infection status (12.9% in uninfected vs. 28.0% in HIV vs. 37.3% in HCV vs. 22.8% in HIV/HCV patients; $P < 0.001$). In the 900 subjects who were not vaccinated, there were significant differences in the types of barriers according to infectious status (see table).

Conclusions:

1. Although HIV/HCV coinfecting patients were more likely to be vaccinated than uninfected patients, there were no more likely to receive the vaccine than those with either HIV or HCV mono-infection.
2. There are marked differences in the types of barriers to HAV vaccination.
3. Public health programs to increase awareness of HAV vaccination among uninfected, HIV-infected and HIV/HCV coinfection to overcome barriers to immunization are needed.

| Barrier | Uninfected | HIV | HCV | HIV-HCV | P-value |
|--|------------|-------|-------|---------|---------|
| My doctor did not offer the vaccine to me | 67.0% | 69.2% | 54.8% | 73.8% | <0.001 |
| I am afraid of the vaccine | 17.5% | 15.4% | 26.0% | 27.7% | 0.009 |
| I am afraid of needles | 15.0% | 28.8% | 21.2% | 32.3% | <0.001 |
| I don't like visiting the doctor | 8.6% | 15.4% | 15.1% | 10.8% | 0.046 |
| I don't understand why I need the vaccine | 40.4% | 25.0% | 36.2% | 40.0% | 0.15 |
| I was feeling too sick | 3.9% | 21.2% | 7.7% | 11.5% | <0.001 |
| It takes me too long to get to my doctor | 3.0% | 11.5% | 14.4% | 12.3% | <0.001 |
| I did not know about a vaccine against HAV | 70.7% | 78.8% | 62.5% | 46.9% | <0.001 |
| I could not afford to pay for the vaccine | 4.4% | 11.5% | 34.0% | 26.9% | <0.001 |

(The study below reinitiates the importance of quality of medical care in treating a population that is more difficult to treat).

M1857. Outcomes in a Multidisciplinary HIV/Hepatitis C Co-Infection Program: Validation of a Model of Care and Comparison with Major Clinical Trials.

B. S. Zingman; H. Morales; F. Rodriguez; K. Freeman; T. Portzline; R. Cruz; L. Aliaga; R. Yanes; J. Shuter

Background:

A multidisciplinary HIV/hepatitis C (HCV) Co-Infection Program was established in 2003 at the MMC AIDS Center's Center for Positive Living/ID Clinic, an inner city clinic serving a largely poor and minority HIV positive population with 38% HCV co-infection. The staff include a medical director, nurse practitioner, patient educators, psychiatrist, substance use counselor, nutritionist, social worker, and statistician. Validation of this treatment model is needed, including demonstration of outcomes in comparison to major clinical trials of HCV treatment in co-infection.

Methods:

This is a prospective evaluation. Standard treatment durations and dosing of pegylated interferon plus ribavirin by HCV genotype were used. All treated patients are included including those retreated for failure. Early virological response (EVR) =>1 log drop in HCV RNA at 12 wks; early treatment response (ETR) =undetectable HCV RNA at completion of planned treatment; sustained virologic response (SVR) =undetectable HCV RNA >6 months after end of treatment.

All analyses are intention to treat (ITT) with censoring of: those on treatment <12 weeks could not be designated as EVR; EVRs who moved are unevaluable for

ETR; ETRs who moved or are <6 months after ETR (“pending”) are unevaluable for SVR. Overall SVR Rates = %ETR x %SVR.

Results:

As of September 30, 2006, 116 HCV treatment courses were initiated in 114 patients (74% male, 74% Hispanic, 75% HCV genotype 1), with 38 patients in progress (13 under <12 wks treatment).

Treatment outcomes:

| | All Evaluable | Evaluable Geno 1 | Evaluable Geno 2/3/4 |
|-------------------------|---------------------|--------------------|----------------------|
| EVR | 71/102 (70%) | 46/77(60%) | 25/25 (100%) |
| ETR | 36/75 (48%) | 19/57 (33%) | 17/18 (94%) |
| Overall SVR Rate | 31% (95% CI 23-41%) | 15% (95% CI 8-25%) | 87% (95% CI 69-97%) |

The overall SVR rates of the “Program” compare favorably to a 27% SVR rate (14% genotype 1, 73% other genotypes) in Chung NEJM 2004; a 40% SVR rate (29% genotype 1, 62% genotypes 2/3) in Torriani [APRICOT] NEJM 2004; and a 27% SVR rate (17% genotypes 1/4, 44% genotypes 2/3/5) in Carrat [RIBAVIC] JAMA 2004.

Conclusions:

- The Montefiore HIV/HCV Co-Infection Program’s multidisciplinary approach demonstrates outcomes comparable to major U.S. and international studies of HCV treatment in co-infected patients.
- The Program’s results are especially notable given its inner-city population and inclusion of some with previous treatment failure.



- The data suggest that this model, if widely replicated, could improve HCV treatment outcomes among co-infected patients.

(To my knowledge, this is the first study of the prevalence of HCV in the Arab American community. This study adds important information to the growing body of evidence that has found a higher prevalence of HCV in many minority populations in the U.S.)

M1024. Prevalence of Hepatitis C Among Arab & Chaldean Americans in Southeast Michigan.

L. H. Jamil; M. C. Duffy; M. Fakhouri; E. Barkho; R. Khoury; H. Fakhouri; H. Jamil

Background:

The prevalence of hepatitis C antibodies (anti-HCV) in the U.S. ranges is approximately 1.6%, with a higher prevalence among African Americans and Hispanics. Patients from Middle Eastern countries may have additional risk factors for hepatitis C Virus (HCV) transmission, such as reusing needles for medical therapy, circumcision by informal health care providers, folk and traditional medical procedures, etc. There are no published studies on the prevalence of anti-HCV among the Arab/Chaldean (belonging to the Chaldean Catholic Church) American population in the U.S.

Methods:

Retrospective review of data collected during an HCV public awareness and education program conducted by the Arab American and Chaldean Council (ACC), a non profit organization, in the Arab/Chaldean American population residing in Southeast Michigan. Inclusion criteria were anti-HCV positive subjects of Arabic/Chaldean descend, born in an Arab country but residing in Metropolitan

Detroit who underwent HCV antibody testing (Home Access Hepatitis C Test). Subjects with an “Indeterminate result” were excluded from further analysis.

Results:

A total of 492 subjects’ data from 62 different zip codes in southeast Michigan, were reviewed. Analysis was performed on 484 subjects. Excluded subjects were either born in the U.S (8), not of Arab/Chaldean descend (3), or tested indeterminate (2). Mean age was 43.2 years (range 18-77 years), males were 50.1%, and 30% did not speak English. The mean number of years of residence in the U.S was 10.4 (range 0.5-52 years).

The overall prevalence of anti-HCV was 5.4%, of whom 44% were male and 60% were between the age of 40-49. The majority of positives were Arabic (96%) and one Chaldean (out of 50 Chaldeans). Highest prevalence was among Jordanians (18.2%) followed by Tunis (16.7%), Egyptians (10%) 105).

Six subjects (24%) reported having an episode of “hepatitis”, and 3 subjects were previously told they had hepatitis C. Four subjects recall having been jaundiced. (20%) reported jaundice.

Reported risk factors included: 72 had a history of IVDA, 62% admitted to risky sexual behaviour, 54% have shared personal hygiene products, 24% had received a blood transfusion, 13% have received an injection by a non-sterile needle, and 14% have had some form an operations. Of the 6 subjects with a history of blood transfusion, 4 of them had the transfusion prior to 1992. The other 2 had their transfusions in the U.S. after 1992.

Discussion:

This is the first study to examine the prevalence of anti-HCV among the Arab and Chaldean Americans in the U.S. These individuals have a much higher prevalence of HCV antibody (5.4%) than the general American population. The 1990 U. S. census found 870,000 Americans who listed “Arab” as one of their top two ancestries. This number is likely higher, given the overall growth of the U.S. and the fact that many may not list ancestries for various reasons. It is estimated that there are 3 to 5 million Arab-Americans residing in the U.S. today. It is not known how many of those were born abroad or in the U.S. Based on our prevalence of anti-HCV of 5.4%, we estimate that between 156,000 to 260,00 Arab/Chaldean Americans are anti HCV positive. With an estimated persons ever being infected nationwide being 4,060,000, up to 6% or more of anti-HCV positive in this relatively small ethnic community that has not been studied. Today, Arab/Chaldean Americans, like many minority groups, are geographically concentrated. Over 2/3 live in ten states: one-third in California, New York, and Michigan. They are also more likely than other Americans to live in large metropolitan areas. Thirty-six percent of Arab-Americans are found in ten cities -- primarily Detroit, New York, or Los Angeles. Minorities in general are less likely to receive preventive medicine and may therefore be less likely to be diagnosed with hepatitis C and receive treatment once identified. In addition, primary care physicians may be less likely to test for HCV in these individuals because of a general lack of awareness of the increased prevalence of anti-HCV in this population. Further studies are needed to better address the communities the communities need s and further public health about HCV in needed in this population.

Conclusion:

- Prevalence of Anti-HCV is 5.4% in the Arab/Chaldean American Community residing in SE Michigan, triple the national average.
- Among those testing positive, 46% were male, 61.5% were between 40-59 years of age, 69% had less than or equal to years of education, and 65% had no health insurance.
- Risk factors: IVDA 72%, 62% risky sexual behaviour, 52% shared personal hygiene products, 15% had received a blood transfusion prior to 1992, and 13% have received an injection by a non-sterile needle.

(There have been a lot of studies on HIV/HCV coinfection, but interestingly very little studies on HCV/HGV coinfection. The study below is good news for people coinfecting with HGV and HCV since HGV does not seem to have an impact on HCV disease progression or HCV treatment response.)

M1005. Prevalence and clinical significance of hepatitis G virus coinfection in patients with chronic hepatitis C undergoing antiviral therapy.

H. Hofer; M. Schoeniger-Hekele; C. Mueller; C. Gurguta; P. Steindl-Munda; P. Ferenci

Background:

Hepatitis G virus (HGV) infection per se is not associated with liver disease. Coinfection with HGV in patients with chronic hepatitis C (CHC) may influence the clinical course and response rates of antiviral therapy with interferon plus ribavirin.

Aim:

The aim of the study was to investigate the prevalence of HGV coinfection and outcome of antiviral combination therapy in HGV/HCV coinfecting patients.

Patients:

Three hundred and four patients with chronic hepatitis C (m=93, age: 42 [18-65] median) were investigated. These patients participants from previous randomized controlled trials. HGV RNA (viral load) detection was done by polymerase chain reaction (PCR) prior to initiation of interferon plus ribavirin combination therapy with standard (N=111) or pegylated interferon (N=193) and after six month--the follow up period. A pre-treatment liver biopsy was done and stage of fibrosis was determined according to the metavir scoring system.

Results:

A HGV/HCV Co-infection could be identified in 37 (12.2%) out of 304 patients (available data).

The predominant HCV-genotype in HGV coinfecting individuals was HCV-2a (51.4%) and the most common source of infection was intravenous drug abuse (N=21). HGV coinfection was more common in patients with HCV-3 compared to HCV-1 or HCV-4 (19/52 (36.5%) vs. 14/187 (7.5%) vs. 4/61 (6.5%), $p < 0.01$).

As compared to patients with HCV infection alone, patients with HGV/HCV coinfection were younger age (mean - 35 (18-56)) vs. mean 41 (19-65); $p < 0.01$) and advanced fibrosis (F3-F4) was less frequent (21.6% vs. 33%, $p < 0.05$).

A sustained virological response (undetectable HCV-RNA) was achieved in 26/34 [76.5%]--HCV- genotype 3a: 14/16 (87.5%); HCV- genotype 1: 9/14 (64.2%), HCV- genotype 4: 3/4 (75%) HGV/HCV co-infected patients as compared to

116/222 (52.3%)--HCV-genotype 3a: 22/26 (84.6%), HCV- genotype 1: 63/147 (42.8%), HCV-gentoype 4: 31/47 (65.9%)) in monoinfected patients ($p < 0.01$).

After antiviral treatment HGV RNA became undetectable in 23/32 (71.8%) patients. In patients with still detectable HGV RNA (but a sustained virological response of HCV) (N=4), ALT levels remained within the normal range at the end of follow-up.

Discussion/Conclusion:

Intravenous drug abuse is a major risk factor for HGV coinfection in patients with chronic hepatitis C. Coinfection with HGV does not aggravate clinical course of chronic hepatitis C or diminish response of HCV to antiviral therapy. Due to the younger age, less fibrosis and the high frequency of HCV -3a HGV conected patients show a favourable response to antiviral combination therapy. Interferon plus ribavirin combination therapy also clears HCV infection in a high proportion of cases.

(Information about the influence of metabolic syndrome on HCV treatment outcomes was one of the highlights of the conference for me. This study validates the strong relationship between metabolic syndrome and treatment outcomes. There are studies that are on-going that are looking at how metabolic syndrome affects HCV disease progression and treatment outcomes and hopefully will outline some steps that people can take to dramatically increase their chances for successful treatment).

M1808. Metabolic Syndrome Is A Strong Predictor Of Treatment Failure In Patients With Chronic Hepatitis C

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Background:

The metabolic syndrome (MS) is a unique pathophysiologic condition whose underlying mechanism is related to insulin resistance. In HCV patients undergoing therapy with Peg IFN/RBV, insulin resistance has been linked to treatment failure.

Aims

Our Aims were to estimate the prevalence of metabolic syndrome in HCV patients undergoing anti-viral therapy and to assess its predictive value in treatment outcome.

Methods:

All HCV patients that were treated with Peg IFN/RBV between 2002 and 2004 and had clinical data to assess for metabolic syndrome were identified (n=251).

Metabolic syndrome was defined using the ATP III criteria. Descriptive statistics were computed for all factors. Univariate analysis was performed to compare variables of interest. A logistic regression analysis was performed to study multivariable associations. The final model contained gender, ethnicity, genotype, metabolic syndrome, fibrosis, and steatosis stage.

Results:

Metabolic syndrome was present in 71/252 (28%) patients. Metabolic syndrome was less common in Caucasian patients compared to non-Caucasian patients [49/193 (25%) vs 22/58 (38%), $p=0.063$].

Overall sustained virologic response (SVR) was achieved in 121/252 (48%) patients. Genotype 1 ($p<0.001$), non-Caucasian ethnicity ($p<0.001$), male gender

($p=0.04$), higher fibrosis stage ($p=0.03$), higher BMI ($p=0.013$), and MS ($p<0.001$) were significantly associated with lack of SVR.

Adjusting for ethnicity, genotype, gender, fibrosis, and steatosis stage, subjects with metabolic syndrome are more likely to fail treatment than those without metabolic syndrome.

Conclusion:

- Metabolic syndrome is frequently seen in patients with hepatitis C and associated with steatosis and advanced fibrosis.
- Consistent with previous studies, genotype 1 non-Caucasian ethnicity and advanced fibrosis are independent, predictors of poor response to pegylated interferon plus ribavirin therapy.
- Metabolic syndrome appears to be an independent **strong** predictor of failure to achieve SVR.
- If confirmed, metabolic syndrome could be easily incorporated into clinical practice to identify HCV patients who are less likely to benefit from antiviral therapy.