



Université Lille 2
Droit et Santé

UNIVERSITÉ DU DROIT ET DE LA SANTÉ - LILLE 2
FACULTE DE MEDECINE HENRI WAREMBOURG
Année : 2021

THÈSE DE DOCTORAT
Spécialité santé publique
Ecole doctorale biologie de la santé

**Déterminants du recours à la vaccination
antigrippale pendant la grossesse**

Présentée et soutenue publiquement le 24/09/2021 à 16h30
au Pôle Formation
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Remerciements :

Je tiens à remercier Mme Odile Launay et M. Laurent Mandelbrot qui ont accepté d'être les rapporteurs de ce travail, ainsi que Mme Karine Faure, Mme Olivia Anselem et M. Rodrigue Dessein d'avoir accepté d'être membre du jury et d'évaluer mon travail. Je vous témoigne ici ma gratitude et mon profond respect.

Je souhaite exprimer ma grande reconnaissance à mon directeur de thèse.

À Damien Subtil, je vous remercie de m'avoir accompagnée tout au long de mon parcours, depuis mon tout début d'internat. Je vous remercie pour votre confiance, vos enseignements, vos encouragements et votre soutien permanent. J'ai énormément appris à vos côtés sur tous les plans.

Je souhaite remercier particulièrement Ophélie Mancel, Emilie Deliege, Aude Lemeret et Sophie Carpentier qui m'ont apporté une grande aide par leur précieuse expertise et les riches échanges que nous avons eus. Ces travaux n'auraient jamais pu voir le jour sans cette riche collaboration.

Je souhaite également remercier Solenne Martinez pour sa gentillesse et sa relecture attentive.

Enfin, un grand merci à ma famille pour leur soutien sans faille, leur confiance et leur amour.

Résumé :

Contexte : Bien que la vaccination des femmes enceintes contre la grippe soit recommandée en France, la couverture vaccinale antigrippale reste très faible.

Objectif : Identifier les déterminants du recours à la vaccination antigrippale et ceux d'une bonne connaissance concernant la grippe et la vaccination antigrippale chez les femmes enceintes ; chez les professionnels de santé : identifier les connaissances, les pratiques et les freins à la vaccination antigrippale.

Matériel et Méthodes : Deux études prospectives observationnelles ont été réalisées durant la saison grippale 2014/2015. La première a été effectuée par auto-questionnaires auprès de toutes les femmes venant d'accoucher dans notre maternité universitaire ; la seconde a été menée à l'aide d'auto-questionnaires adressés à tous les professionnels de santé de notre réseau de périnatalité.

Résultats : Parmi les 2045 femmes incluses dans notre étude (87%), 35% ont déclaré avoir été vaccinées contre la grippe pendant leur grossesse. Les déterminants du recours à la vaccination étaient : une vaccination antérieure contre la grippe, la nulliparité, un antécédent d'accouchement prématuré <34 SA, la perception que la fréquence des complications du vaccin est très faible chez le bébé, une bonne connaissance concernant la grippe et la vaccination antigrippale, une recommandation vaccinale par un professionnel de santé, avoir reçu le formulaire de remboursement et avoir été informée par au moins un professionnel de santé. Les déterminants d'une bonne connaissance étaient : un âge supérieur à 24 ans, un haut niveau d'éducation, un antécédent de vaccination contre la grippe, la nulliparité et une recommandation vaccinale par un professionnel de santé. Les 144 professionnels ayant répondu à notre questionnaire (41%) avaient des bonnes

connaissances. Les principaux freins qu'ils rencontraient étaient le refus des patientes (54%), un manque de connaissance de leur part (32%) et un manque de temps (21%).

Conclusion : La couverture vaccinale des femmes enceintes semble liée à plusieurs facteurs. Notre travail invite à mener des actions à destination des femmes enceintes, mais surtout des professionnels de santé qui les prennent en charge. Il s'agira d'améliorer leurs connaissances concernant la gravité de la maladie, l'efficacité du vaccin pour la mère et pour le bébé, ainsi que sa prise en charge totale par l'Assurance Maladie.

ABSTRACT:

Background: Although vaccination of pregnant women against influenza is recommended, the vaccination rate remains low. We have conducted a study to identify determinants of influenza vaccination uptake in pregnancy, determinant of a good knowledge and knowledge, practices and barriers reported by healthcare professionals with regard to influenza vaccination during pregnancy.

Methods: We have conducted 2 studies. The first one was a prospective observational hospital-based study in the French hospital, performing the highest number of deliveries among all women who had given birth during the 2014–2015 influenza season. Data were collected through a self-completed survey and from medical files. Determinants of vaccination uptake and of a good knowledge were identified using logistic regression analysis. The second study was a prospective,

observational, self-questionnaire-based study of healthcare professionals in a mother & child health network during the same period.

Results: Among the 2045 women concerned by the study, 35.5% reported that they had been vaccinated against influenza during their pregnancy. The principal factors significantly associated with greater vaccination uptake were previous influenza vaccination, nulliparity, history of preterm delivery <34 weeks, the mother's perception that the frequency of vaccine complications for babies is very low, the mother's good knowledge of influenza and its vaccine, vaccination recommendations during pregnancy by a healthcare worker, receipt of a vaccine reimbursement form, and information from at least one healthcare worker about the vaccine. Determinants of the highest level of knowledge were age over 24, a high educational level, previous influenza vaccination, nulliparity, and the recommendation of vaccination by a healthcare professional. According to the 144 respondents, the main reported barriers to vaccination were refusal by the patient (54%), the healthcare professional's admitted lack of knowledge about influenza and the influenza vaccine (32%), and a lack of time (20%).

Conclusions: Our findings suggest that, in order to increase flu vaccination compliance among pregnant women, future public health programs must ensure cost-free access to vaccination, and incorporate education about the risks of influenza and the efficacy/safety of vaccination and clear recommendations from healthcare professionals into routine antenatal care.

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Introduction :

I. Epidémiologie de la grippe :

La grippe est une infection aiguë des voies aériennes supérieures d'origine virale, due au Myxovirus influenzae appartenant à la famille des *Orthomyxoviridae*. Il s'agit d'un virus à ARN enveloppé dont il existe 4 types : A, B, C et D. Chez l'humain, ce sont les virus grippaux de type A et B qui sont à l'origine des épidémies saisonnières (1,2). Chacun de ces types fait l'objet de différentes sous-divisions.

Les **virus de type A** touchent l'espèce humaine et sont classés eux-mêmes en sous-types selon les variantes de deux protéines qu'ils portent à leur surface : l'Hémagglutinine (H) et la Neuraminidase (N). À l'heure actuelle, il existe 18 sous-types d'Hémagglutinine et 11 sous-types de Neuraminidase connus (1,2). Ils sont divisés à leur tour en sous-groupes, selon la similitude ou non de leurs séquences de gènes de l'Hémagglutinine. Les **virus de type B** touchent également l'espèce humaine et sont divisés en deux lignages : B/Yamagata and B/Victoria (1,2). Les **virus de type C** peuvent toucher l'espèce humaine, mais ne sont pas responsables d'épidémies. Ils n'entraînent que des symptômes peu sévères (1,2). Enfin, les **virus de type D** affectent principalement les bovins et ne sont pas connus comme étant pathogènes pour l'espèce humaine (2).

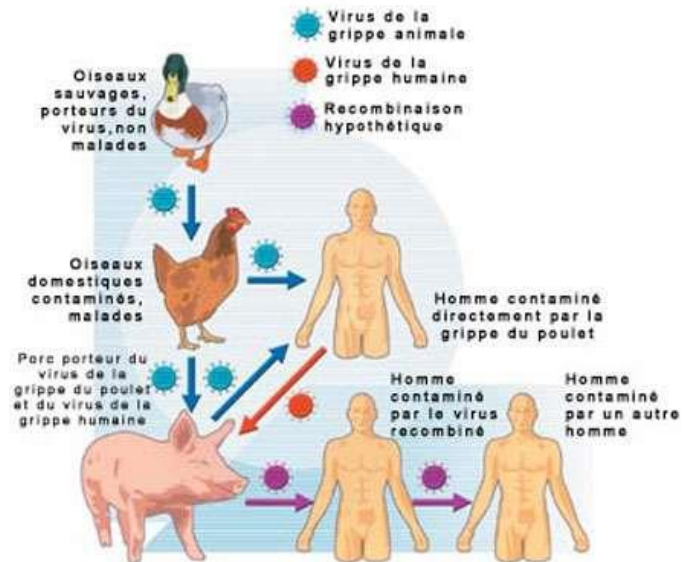
La transmission de la grippe se fait principalement par projection de gouttelettes lors de la toux, l'éternuement ou la parole d'un sujet infecté. Les virus pénètrent ainsi dans l'organisme par voie rhino-pharyngée et respiratoire. Elle peut également se transmettre dans une moindre mesure par un phénomène d'aérosol qui reste en

suspension dans l'atmosphère ou par voie manuportée (lorsqu'un sujet touche une surface contaminée puis porte ses mains à proximité de son nez (1,3)).

Le virus de la grippe sévit sous forme de ***cas isolés***, d'***épidémies*** ou de ***pandémies*** (1,2). Seuls les virus de type A

sont responsables des pandémies.

Ils ont un fort potentiel de mutation antigénique, ce qui fait leur potentielle gravité à l'échelle mondiale. En effet, lorsqu'un virus de type A non-humain - qui se rencontre surtout chez les oiseaux et les cochons - subit une mutation



antigénique majeure, cela peut entraîner la transmission directe d'un virus non humain à des humains (4). Chez les volailles, le virus influenza se multiplie principalement au niveau du tractus digestif, ainsi qu'au niveau du tractus respiratoire. De ce fait, de grandes quantités de virus sont excrétées dans les fientes et contaminent l'environnement. La transmission à l'homme nécessite une exposition prolongée à des volailles infectées ou à des environnements contaminés. Ces mutations antigéniques peuvent également survenir de manière indirecte, lorsqu'un virus de la grippe de type A humain échange des informations génétiques avec un virus de type A non-humain, au sein de l'organisme d'un animal qui porte ces deux virus différents en même temps. Ce phénomène est appelé « réassortiment » ou « recombinaison » (1). Cette mutation est à l'origine d'un nouveau virus, vis-à-vis duquel la majorité de la population n'est pas protégée (1). Celui-ci a la faculté d'infecter des humains et de se transmettre de personne à personne (4).

L'humanité rencontre une grande pandémie grippale tous les 10 à 40 ans. La plus ancienne et l'une des mieux connues est la « grippe espagnole » de 1918, due à un virus aviaire A de sous-type H1N1 d'origine asiatique, mais initialement décrit en Espagne. Cette pandémie a été jugée responsable de 20 à 50 millions de morts entre 1918 et 1919 (1). Puis, il y eut la « grippe asiatique » de 1957, due à un virus A de sous-type H2N2, qui aurait été responsable d'environ 1 million de décès. Ensuite, la « grippe de Hong Kong » de 1968, due au sous-type H3N2, qui aurait été responsable d'environ 800.000 décès. Enfin la pandémie de 2009, pour laquelle le virus responsable était un nouveau variant de sous-type H1N1 - nommé A(H1N1)pdm09 -, résultant d'une recombinaison entre un virus humain, un virus aviaire et deux virus porcins. Elle a été responsable d'environ 18 500 décès confirmés par prélèvements (5) et de 284.500 décès selon des estimations faites *a posteriori* (6). Depuis 2009, ce virus A(H1N1)pdm09 a remplacé les précédents virus A(H1N1). Actuellement, ce virus est co-responsable - avec les virus A(H3N2) et les virus de type B - des épidémies saisonnières actuelles (1).

Les épidémies sont annuelles, mais il n'est cependant pas possible de déterminer ni quand elles vont commencer, ni leur durée, ni les virus qui vont les composer (1). La grippe saisonnière est très contagieuse, puisqu'elle a un taux d'attaque de 5 à 10% chez l'adulte et de 20 à 30% chez l'enfant (7,8). Les températures froides favorisent la survie des virus grippaux, ce qui explique la répartition planétaire des épidémies. Celles-ci surviennent en effet généralement de Novembre à Avril dans les pays tempérés de l'hémisphère Nord, et principalement entre Avril et Octobre dans l'hémisphère Sud (1). Dans les pays tropicaux et subtropicaux, les virus grippaux circulent toute l'année (1,2).

II. Morbi-mortalité de la grippe :

La grippe se manifeste principalement par une fièvre d'apparition brutale, des douleurs musculaires, des céphalées, une sensation de malaise et des signes respiratoires tels qu'une toux sèche et une rhinite, qui durent en général une semaine et apparaissent 1 à 4 jours après la contamination (1,9). Elle peut entraîner des complications respiratoires et extra-respiratoires. Les pneumonies peuvent être dues au virus de la grippe lui-même, ou bien à une surinfection bactérienne. La grippe peut également entraîner des myocardites, des encéphalites, des myosites ou rhabdomyolyses et des défaillances multi-viscérales, mais également la décompensation d'une pathologie chronique préexistante (9). De plus, elle peut être responsable de formes sévères qui se définissent par la nécessité d'une hospitalisation, voire par le décès du sujet infecté, surtout chez des sujets à risques.

En France, les personnes à risque de grippe sévère sont définies comme (10) :

- Les personnes âgées de 65 ans et plus,
- Les personnes avec des pathologies chroniques respiratoires, cardiaques, neurologiques, rénales, hépatiques, du diabète de type 1 ou 2, des déficits immunitaires primitifs ou acquis,
- Les personnes obèses avec un Indice de Masse Corporel (IMC) supérieur ou égal à 40 kg/m²,
- Les femmes enceintes, quel que soit le trimestre de la grossesse,
- Les nourrissons de moins de 6 mois.

L'Organisation Mondiale de la Santé (OMS) ajoute à cette liste les enfants de moins de 5 ans (11).

En France, la grippe saisonnière touche 2 à 8 millions de personnes et est responsable de 10 000 à 15 000 décès chaque année (1). Aux Etats-Unis, la grippe aurait touché 38.000.000 personnes durant la saison 2019-2020, et aurait entraîné 400.000 hospitalisations et 22.000 décès dans le même temps (3). L'OMS estime que les épidémies annuelles de grippe causent environ 3 à 5 millions de formes sévères de la maladie de par le monde, ainsi qu'entre 290 000 et 650 000 décès par pathologie respiratoire (11).

III. Morbi-mortalité chez les femmes enceintes du fait de la grippe :

Les femmes enceintes font partie des sujets à risque, car elles présentent plus souvent des formes sévères de la maladie et sont plus à risque d'hospitalisation et de décès (12–14). Ce phénomène a été mesuré en cas de pandémie, mais également en cas de grippe saisonnière. Pendant la grippe « espagnole » de 1918, le taux de décès des femmes enceintes contaminées par la grippe a atteint 27 % (15). Récemment, lors de la pandémie grippale H1N1 de 2009, 5% des décès sont survenus chez les femmes enceintes, alors même qu'elles ne représentaient qu'environ 1% de la population (16). Plusieurs études ont retrouvé une surmortalité liée à la grippe saisonnière. En 2017, une méta analyse retrouvait des RR de décès liés à la grippe, allant de 3.9 à 50 dans la littérature (13), avec un risque de mortalité plus important au 3^e trimestre (14,16,17). Les femmes enceintes présentent 4 fois plus de risque d'être hospitalisées pour grippe que la population générale (12).

La raison de cette susceptibilité particulière des femmes enceintes – notamment au 3^e trimestre – est mal connue et probablement multifactorielle (14,18). Elle résulte de

la triple susceptibilité cardiaque, respiratoire et immunologique des femmes enceintes.

La susceptibilité cardiaque des femmes enceintes est bien connue et principalement liée à l'augmentation du débit cardiaque nécessitée par l'expansion de 30 à 50% du volume sanguin, où le volume utérin à perfuser atteint 600 millilitres chaque minute en fin de grossesse (19,20). C'est principalement à cette période que surviennent les décompensations de cardiopathies préexistantes (19). C'est également là que surviennent les œdèmes aigus du poumon (OAP), qui peuvent être déclenchés par un simple traitement inhibiteur calcique ou bêtamimétique, notamment en cas de grossesse gémellaire (21,22).

La susceptibilité respiratoire des femmes enceintes semble à la fois mécanique et fonctionnelle. D'un point de vue mécanique, la sécrétion massive d'HCG et de progestérone entraînerait une modification de la forme et de la dimension du thorax (18), à laquelle s'associe une élévation du diaphragme liée à l'augmentation de volume de l'utérus gravide (18). Ces modifications entraînent chez la plupart des femmes une sensation de dyspnée dont le pic est atteint au début du 3^e trimestre (18). À ces modifications mécaniques s'ajoutent des modifications fonctionnelles, puisque la consommation en oxygène augmente de 15 à 20%, avec une augmentation de 30 à 40% du volume courant (18) et une alcalose respiratoire compensée (23).

Enfin, la grossesse est associée à une diminution de l'immunité cellulaire, une diminution de nombre des lymphocytes T Helper, une diminution de l'activité des lymphocytes Natural Killer et une diminution de l'activité cytotoxique des lymphocytes (24,25). Ces modifications sont dues à des interactions complexes et multifactorielles

entre les hormones sexuelles et le système immunitaire (25). Par ailleurs, la forte expression de HLA-G à la surface du syncytiotrophoblaste joue un rôle dans la tolérance immunitaire materno-fœtale en inhibant l'activité lytique des cellules NK maternelles. L'expression par le virus A/H1N1 d'antigènes « HLA-G like », pourrait également expliquer la survenue de formes graves de grippe chez la femme enceinte (26).

IV. Prématurité et mortalité périnatale :

Alors qu'un risque augmenté de prématurité et de mortalité périnatale avait été évoqué jusqu'ici (27,28), les risques fœtaux et néonataux liés à la grippe semblent être actuellement remis en question (29,30). Pour ce qui concerne le risque d'accouchement prématuré, une méta analyse récente portant sur 16 études retrouvait des Odds Ratio (OR) très variables, compris entre 0.40 à 4.08 (29). L'hétérogénéité entre ces 16 études était très importante. Parmi elles, seulement quatre retrouvaient une augmentation significative du risque d'accouchement prématuré, allant de 2.39 à 4.08. Concernant le risque de Petit poids pour l'Age Gestationnel (PAG), l'OR poolé était de 1.7 IC95% [0.96-1.59]. Le risque de mort fœtale a également été étudié, avec une hétérogénéité dans la définition de la mort fœtale et des résultats très variables avec des OR allant de 0,40 à 12,50 (29). Une méta-analyse plus récente a montré l'existence d'une augmentation du risque de mortalité néonatale RR=3.62, IC95%[1.60-8.20], mais sans augmentation du risque de mortinatalité, RR 0.93, IC95%[0.73-1.18](31). Cet excès de mortalité néonatale peut être mis en rapport avec l'excès de mortalité modéré lié aux gripes néonatales, rares mais potentiellement graves (32).

V. Vaccination antigrippale :

Les vaccins sont fabriqués par culture de virus au sein de cellules en culture ou d'œufs embryonnés (33). Il s'agit le plus souvent de vaccins quadrivalents inactivés contenant 2 souches grippales A et 2 souches grippales B (1). Il existe également des vaccins trivalents contenant 2 souches grippales A et 1 souche grippale B. Ils doivent être conservés entre 2 et 8°C, protégés de la lumière, et s'injectent en intra musculaire.

Les vaccins antigrippaux inactivés apparaissent sans danger maternel ni fœtal. Leurs effets indésirables les plus fréquemment rencontrés sont une réaction locale au niveau du point d'infection et un syndrome pseudo-grippal (>1/100) (34). La sûreté du vaccin est attestée par une étude décrivant les effets indésirables rapportés au Vaccine Adverse Event Reporting System (VAERS) qui assurait la surveillance post commercialisation des vaccins aux Etats-Unis, de 1990 à 2005. Le syndrome de Guillain Barré est l'évènement indésirable sévère le plus fréquemment rapporté avec un taux de 0,70 par million de vaccins (34). Concernant les effets indésirables de la vaccination antigrippale pendant la grossesse, une étude des données du Vaccines and Medications in Pregnancy Surveillance System (VAMPSS) de 2010 à 2014 ne retrouvait pas de sur risque de malformation fœtale, de fausse couche, de petit poids pour l'âge gestationnel (35), ou d'accouchement prématuré (36).

Récemment, en Novembre 2020, l'European Medicines Agency (EMA), a autorisé l'utilisation d'un vaccin quadrivalent recombinant chez les personnes de plus de 18 ans (37).

Il existe également des vaccins vivants atténués qui s'administrent par voie nasale, mais ceux-ci ne sont pas commercialisés en France; sauf en cas de contexte exceptionnel de tension d'approvisionnement (38) et ils sont contre-indiqués pendant la grossesse.

Deux arguments militent en faveur du caractère annuel de la vaccination. Le premier est que la protection conférée par les vaccins antigrippaux a une durée relativement courte, estimée entre 6 et 9 mois (1,33). Le second est de pouvoir garantir une correspondance optimale entre le vaccin et les souches prévalentes. En effet, compte tenu du potentiel de mutation important du virus, la composition des vaccins est revue 2 fois par an et ajustée en fonction des données recueillies par le système de surveillance et de réponse mondiale de la grippe de l'OMS (Global Influenza Surveillance and Response System (GISRS)) (33).

VI. Vaccination antigrippale chez la femme enceinte

Malgré le fait que la grossesse entraîne les modifications du système immunitaire vues plus haut, la vaccination antigrippale de la femme enceinte permet d'un autre côté d'obtenir une bonne immunogénicité (39–42). Après l'administration d'un vaccin trivalent inactivé, Madhi et al retrouvent des taux de séroconversion de 72,5% pour le virus A H1N1 pdm09, de 64,8% pour le virus A H3N2 et de 92,5% pour le virus B Victoria (39).

Cette efficacité sérologique s'accompagne d'une réduction des cas de grippe, dont le niveau diffère selon les études. Ces différences s'expliquent à la fois par la diversité des souches selon les vaccins et les pays, mais également par le fait que certaines

études comptabilisent tous les cas de grippe survenus cliniquement chez des femmes enceintes (27) ; tandis que d'autres portent seulement sur ceux qui surviennent chez des femmes enceintes hospitalisées (43) ; et d'autres encore, seulement sur les cas confirmés par RT-PCR (39). Ainsi, quand Haberg et al retrouvaient une efficacité vaccinale de 70% en considérant le diagnostic clinique de grippe parmi 117,347 femmes enceintes IC95 [65%-75%] (27), Madhi et al retrouvaient une réduction de l'efficacité vaccinale de seulement 50,4% IC95 [14,5%-71,2%] chez 2116 femmes enceintes. Parallèlement, entre 2010 et 2016 un travail réalisé à partir de registres hospitaliers d'Australie, du Canada, d'Israël et des Etats-Unis, révélait une efficacité du vaccin de seulement 40%, IC 95% [12%-59%].

Grâce au passage transplacentaire des anticorps obtenus à l'aide de la vaccination, celle-ci apporte également une protection du nouveau-né à la naissance. Un essai contrôlé randomisé qui suivait jusqu'à 6 mois de vie des nouveau-nés de mère ayant reçu soit un placebo soit un vaccin antigrippal, montrait une réduction de 63% des cas de grippe confirmés par prélèvement (44). Dans une analyse secondaire d'un essai contrôlé randomisé réalisé en Afrique du Sud, Nunnes et al retrouvaient une réduction des cas de grippe confirmé par prélèvement de 85,6% chez les nouveau-nés de moins de 8 semaines. Cette protection décroissait ensuite à 25.5% chez les nourrissons de 8 à 16 semaines, certainement du fait de la disparition progressive des anticorps maternels chez l'enfant (40).

VII. Couverture vaccinale antigrippale des femmes enceintes

Même parmi les pays très développés, la couverture vaccinale antigrippale des femmes enceintes apparaît très hétérogène. Aux États-Unis durant la saison 2019-

2020, la couverture vaccinale de la femme enceinte était mesurée à 61,2% ; soit une augmentation de 7,5% par rapport à la saison précédente (45).

En Europe, L'European Centre for Disease prevention and Control (ECDC) a récemment réalisé une étude sur la politique et la couverture vaccinale de 30 pays de l'Union Européenne durant les saisons 2015-2016, 2016-2017 et 2017-2018. Parmi les 30 états membres ayant participé, 28 recommandaient la vaccination antigrippale chez la femme enceinte. Parmi les 9 états membres pour lesquels la couverture vaccinale était disponible (Belgique, Finlande, Hongrie, Irlande, Italie, Lituanie, Roumanie, Slovénie, Royaume-Uni), celle-ci allait de 0,5% à 58,6%, avec une médiane de 25% (46). Avec une couverture vaccinale mesurée à 7% chez les femmes enceintes durant la saison 2015-2016. La France apparaît donc très en retard par rapport à ses voisins européens (47).

Objectifs :

Le but de ce travail était de comprendre les raisons de la faiblesse de la couverture vaccinale contre la grippe chez les femmes enceintes ; ceci afin de dégager des pistes d'amélioration possibles. Notre hypothèse était en particulier que les femmes enceintes et les professionnels de santé avaient peut être un manque de connaissances concernant la vaccination antigrippale et les risques de la grippe pendant la grossesse.

Ceci nous a conduit à définir les objectifs suivants :

- Identifier les déterminants du recours à la vaccination antigrippale pendant la grossesse ; puis les déterminants d'une bonne connaissance de la grippe et de la vaccination antigrippale chez les femmes enceintes elles-mêmes,
- Identifier les connaissances, les pratiques et les freins à la vaccination antigrippale chez les professionnels de santé prenant en charge des femmes enceintes.

Matériel et méthodes :

Pour atteindre nos objectifs, deux études observationnelles ad hoc ont été menées durant la saison grippale 2014-2015 : l'une à destination des femmes enceintes, l'autre à destination des professionnels de santé.

La **première étude** était à destination des femmes enceintes, observationnelle unicentrique. Elle a été menée à l'aide d'auto-questionnaires proposés de manière prospective à des femmes venant d'accoucher dans une maternité universitaire de type 3. Cet auto-questionnaire a été élaboré sur la base de celui-proposé par Yudin et al afin d'explorer le recours à la vaccination chez la femme enceinte (48) et a été modifié par un comité d'expert pluridisciplinaire comportant au moins un membre des disciplines suivantes : gynécologie-obstétrique, maladies infectieuses, pédiatrie, médecine générale, épidémiologie. Il portait sur la grippe en général et pendant la grossesse, la vaccination antigrippale et ses risques éventuels pour la mère et le fœtus, l'existence ou non d'une proposition vaccinale et/ou d'une remise d'un formulaire de remboursement au cours de la grossesse, la réalisation ou non d'une vaccination antigrippale et les raisons de ce choix (Annexe 1). L'organisation de l'étude voulait que cet auto-questionnaire soit remis et accompagné d'un mot d'explication en « face à face » à toutes les femmes présentes dans le service de suites de couches de la maternité universitaire durant la période d'inclusion. Les données médicales étaient extraites du dossier obstétrical des patientes.

Articles :

I. Article 1 :

Le doctorant a participé à l'élaboration de la méthodologie de l'étude, à la création du questionnaire, au data management, à l'analyse des résultats et à l'écriture de l'article.

Cette première étude a donné lieu à deux analyses différentes et complémentaires : l'une destinée à mettre en évidence les déterminants de la vaccination chez les femmes enceintes; l'autre à déterminer les facteurs liés à une bonne connaissance de la grippe et de la vaccination antigrippale chez elles. Chacune de ces deux études fera l'objet d'une publication.

Determinants of influenza vaccination uptake in pregnancy: a large single-centre cohort study.

ABSTRACT:

Background: Although vaccination of pregnant women against influenza is recommended, the vaccination rate remains low. We conducted a study to identify determinants of influenza vaccination uptake in pregnancy in order to identify strategies to improve seasonal influenza vaccination rates.

Methods: Prospective observational hospital-based study in the French hospital performing the highest number of deliveries, located in the city of Lille, among all women who had given birth during the 2014–2015 influenza season. Data were collected through a self-completed questionnaire and from medical files. The vaccination uptake was self-reported. Determinants of vaccination uptake were identified using logistic regression analysis.

Results: Of the 2045 women included in the study, 35.5% reported that they had been vaccinated against influenza during their pregnancy. The principal factors significantly associated with greater vaccination uptake were previous influenza vaccination (50.9% vs 20.2%, OR 4.1, 95% CI 3.1-5.5), nulliparity (41.0% vs 31.3%, OR 2.5, 95% CI 1.7-3.7), history of preterm delivery <34 weeks (43.4% vs 30.3%, OR 2.3, 95% CI 1.1-4.9), the mother's perception that the frequency of vaccine complications for babies is very low (54.6% vs 20.6%, OR 1.1, 95% CI 0.5-2.2), the mother's good knowledge of influenza and its vaccine (61.7% vs 24.4%, OR 3.1, 95% CI 2.2-4.4), hospital-based prenatal care in their first trimester of pregnancy (55.0% vs 30.2%, OR 2.1, 95% CI 1.2-3.7), vaccination recommendations during

pregnancy by a healthcare worker (47.0% vs 2.7%, OR 18.8, 95% CI 10.0-35.8), receipt of a vaccine reimbursement form (52.4% vs 18.6%, OR 2.0, 95% CI 1.5-2.7), and information from at least one healthcare worker about the vaccine (43.8% vs 19.1%, OR 1.8, 95% CI 1.3-2.6).

Conclusions: Our findings suggest that in order to increase flu vaccination compliance among pregnant women, future public health programmes must ensure cost-free access to vaccination, and incorporate education about the risks of influenza and the efficacy/safety of vaccination and clear recommendations from healthcare professionals into routine antenatal care.

Trial registration: committee for ethics in research in gynaecology and obstetrics, n° CEROG OBS 2014-11-01

Keywords: Influenza vaccine, pregnancy, health knowledge, behaviours

INTRODUCTION:

Seasonal influenza is a common and contagious illness with an annual attack rate estimated at 5%–10% in adults, pregnant women being at increased risks of morbidity and death (33), even those with no comorbidities (49).

Seasonal influenza vaccination during pregnancy reduces the risk of an influenza diagnosis by 50% (39). It also confers effective protection up to the age of 6 months for newborns whose mother was vaccinated during pregnancy (42) with a reduction of 63% in influenza cases and of 29% in episodes of febrile respiratory illness (44). A review of 15 years of surveillance data covering 750 million doses of the vaccine in the United States revealed no data that raised concerns about its safety in general population (34), neither for the foetus nor the mother, as showed by other studies (35,36,50,51). As a result, the World Health Organization (WHO) (33), the American College of Obstetricians and Gynecologists and the Centers for Disease Control and Prevention (CDC) (52), recommend seasonal influenza vaccination for pregnant women, regardless of gestational age.

Several previous studies have identified factors affecting pregnant women's decisions about whether to get a seasonal influenza vaccination (53–57). Despite this, the vaccination coverage in pregnant women remains very low: 7% in France in 2016 (47), 45% in England in 2017 (58), and 37% in the US in 2017 (59) and lower than the Healthy People 2020 target of 80% (60). Therefore, to explore why the vaccination coverage remains very low, we conducted one of the largest cohort studies on this topic to date to evaluate women motivations to be vaccinated or not. We also investigated a large number of possible determinants, in order to find strategies to improve seasonal influenza vaccination rate.

MATERIAL AND METHODS:

- Study design and sampling method:

We conducted a prospective single centre observational study during the 2014–2015 influenza season in a level-III University maternity unit in Lille, France, with an approximate birth rate of 5000 births/year. In France, women must obtain a prescription and a reimbursement form from their general practitioner or antenatal care provider, purchase the vaccine from a drugstore and the vaccine may then be administered during another appointment with the healthcare worker conducting the antenatal care or by a nurse at home. The vaccine is cost-free if the woman provides the drugstore with a reimbursement form. Eligible women for the study were all the women giving birth in our maternity unit and having received prenatal care during the 2014–2015 vaccination campaign between November 17, 2014, and June 5, 2015. The study excluded those younger than 18 years, or who did not speak French, or had a contraindication to the influenza vaccination, or refused to participate. For all participants written consent was obtained.

- Variables considered in our study:

The outcome of interest was seasonal influenza vaccination uptake, reported by the pregnant women as part of a self-completed questionnaire. Data were collected from medical forms and from a self-completed paper questionnaire offered by the clinical staff to all eligible women during their postpartum hospitalisation. Variables considered as possible determinants of vaccine uptake were

1. maternal sociodemographic characteristics: age, educational level and living or not with her partner;

2. maternal medical characteristics before pregnancy: pre-existing comorbidities for which influenza vaccination is indicated according to French guidelines (grouped into major categories: respiratory, cardiac, neurological, kidney-related, haematological and immune-related, diabetes, chronic liver disease, and obesity with Body Mass Index (BMI) $\geq 40 \text{ kg/m}^2$ (61)), being vaccinated against influenza before this pregnancy, number of previous deliveries, history of preterm delivery before 34 weeks;
3. characteristics of the current pregnancy: smoking status, obstetrical complications defined as gestational diabetes, gestational hypertension, pre-eclampsia, HELLP syndrome, infections and foetal growth restriction;
4. antenatal care: the starting time of prenatal care at the hospital, the healthcare worker providing the prenatal care being a gynaecologist-obstetrician, general practitioner, hospital midwife, private midwife, profession of the healthcare worker recommending the vaccination, the provision of a reimbursement form for the vaccine;
5. maternal knowledge about influenza and its vaccine: frequency of influenza, knowledge of serious complications of influenza for mothers and their infants, the frequency of vaccine complications for mothers and their infants, knowledge about the recommendation of the vaccine in pregnancy.

Data about maternal sociodemographic characteristics, maternal medical characteristics before pregnancy, and characteristics of this pregnancy were

extracted from the medical forms. Prenatal care and maternal knowledge about influenza and its vaccine were extracted from the self-completed questionnaire. The questionnaire was adapted from the questionnaire used by Yudin et al. to assess women's knowledge of influenza and its vaccination (48). We also created a "knowledge score" about this disease and its vaccine before the study with a multidisciplinary group of experts including obstetricians, infectious disease specialists, general practitioners, and statisticians from the potential responses to the self-completed questionnaire (see additional information). The score ranged from 0 to 9 points and a woman was considered to have good knowledge when her score was higher than the last quartile of the score distribution, that is, a knowledge score greater than 5.4/9 in our study.

- Statistical analyses:

To identify determinants associated with vaccination uptake, we conducted bivariate and multivariate logistic regression analysis. Dependent variables included in the regression model were those previously described as determinants of vaccine uptake in scientific literature or associated with vaccination uptake in bivariate analysis with a *p*-value less than 0.20. We have calculated variance inflation factor to check for multicollinearity and all the variables have a VIF<2.0. In order to evaluate if the profession of the healthcare worker recommending the vaccination was a relevant factor, we conducted an analysis only on women to whom vaccination had been recommended during pregnancy. Percentages were compared using the chi-2 test or Fisher's exact test, depending on the number of individuals. We calculated adjusted odds ratios (aORs) with their 95% confidence interval (95% CI). The difference was considered significant if *p*<0.05. The analyses were performed with

STATA software version 13.0.0 (Copyright 1985–2013 StataCorp LP, StataCorp, College Station, TX, USA).

Our study adheres to the STROBE guidelines. The CEROG (committee for ethics in research in gynaecology and obstetrics, n° CEROG OBS 2014-11-01) approved of this study.

RESULTS:

Of the 2862 women who gave birth during the inclusion period, 370 did not receive the questionnaire (12.9%), 138 were excluded from the study (5.5%), 216 women received the questionnaire but did not return it (9.2%), and 24 women did not answer the question about their influenza vaccination. Therefore, 2045 women (86.9%) were included in the analysis (Figure 1).

One third of the women questioned (35.5%) reported they had been vaccinated against seasonal influenza during their pregnancy. Table 1 presents the maternal factors associated with this vaccination. Women were vaccinated more often if they had at least one comorbidity (40.0%), if they had previously been vaccinated against influenza (50.9%), especially during a previous pregnancy (92.0%), and if they were nulliparous (41.0%). Higher vaccination rates were also observed for women who perceived influenza as a common disease (37.6%), or its vaccination as having a very low rate of complications for mothers (52.3%) or babies (54.6%), and when they had good knowledge about influenza (61.7%). Note that educational level and severe obesity (BMI > 40 kg/m²) were not associated with vaccination.

The prenatal care factors associated with vaccination (Table 2) were hospital-based prenatal care in their first trimester of pregnancy (55.0%), having received a vaccination recommendation (47.0%), especially by a general practitioner (57.3%) or a midwife in private practice (54.3%), receipt of a vaccine reimbursement form (52.4%), or information from a healthcare worker (43.8%).

Women motivations to be vaccinated or not are summarised in table 3. The major motivation to be vaccinated was that the vaccine protects the baby (83%) and

at the second place that the vaccine protects her (73%). A third of the vaccinated women claimed as motivation that they had received sufficient information about the benefits of the vaccine. The reasons not to be vaccinated were more variables: not to have enough information about the benefit and risk of the vaccine (32%), to be rather “against” vaccines in general (26%), to be scared for the baby’s health (24%).

On logistic regression analysis (Table 4), statistically significant determinants of vaccination were a previous influenza vaccination (50.9% vs 20.2%, OR 4.1, 95% CI 3.3-5.5), nulliparity (41.0% vs 30.3%, OR 2.5, 95% CI 1.7-3.7), history of preterm delivery <34 weeks (43.4% vs 35.1%, OR 2.3, 95% CI 1.1-4.9), perception that the frequency of vaccine complications for babies is very low (54.6% vs 35.4%, OR 1.1, 95% CI 0.5-2.2), the mothers’ good knowledge of influenza and the vaccine (61.7% vs 24.4%, OR 3.1, 95% CI 2.2-4.4), hospital-based prenatal care in their first trimester of pregnancy (55% vs 30.2%, OR 2.1, 95% CI 1.2-3.7), vaccination recommendations (47.0% vs 2.7%, OR 18.8, 95% CI 10.0-35.8) and when this recommendation was done by a general practitioner (57.3% vs 50.7% for Gynaecologist-Obstetrician, OR 1.6 CI 1.0-2.8), receipt of a vaccine reimbursement form (52.4% vs 18.6%, OR 2.0, 95% CI 1.5-2.7), and having received information about the vaccine from at least one healthcare worker (43.8% vs 19.1%, OR 1.8, 95% CI 1.3-2.6).

DISCUSSION:

Our study examined the potential determinants of the influenza vaccination uptake amongst pregnant women in a single centre in France.

Overall, our findings highlight the importance of the healthcare worker in vaccination uptake. Indeed, vaccination recommendation by a healthcare provider strongly influence vaccination uptake (aOR 19). In addition to making a recommendation, the influence of healthcare worker was also vital in educating women about the influenza and the vaccine and providing reimbursement form.

Indeed, among factors that may be modified to improve the vaccination rate, we found, similar to other authors, that several are related to knowledge and perception of influenza, its vaccine and its potential complications (48,53,54,56,57,62). Moreover, our study found that protecting the baby against influenza was the leading motivation for vaccination among those pregnant women who were vaccinated (83%). In a systematic review of the literature on the subject, 41% of the articles studied found that vaccine safety was a major concern among pregnant women, for all vaccines combined (63). Furthermore, our study demonstrates the role of healthcare professionals as an essential source of information for the pregnant women who are vaccinated. Inversely, sources of information such as television, radio, the print media, the internet, family and friends are associated with lower vaccination rates in our study and in the literature (57,63,64). Conversely, good knowledge of influenza and its vaccine was closely associated with vaccination among the women questioned in our study. This should provide incentives to implement measures to improve the quality of information provided to women by healthcare worker (54,65).

Concerning the major impact of the recommendation and provision of the reimbursement form by healthcare worker, our results are corroborated by the data from the literature: an analysis by the CDC for the 2016–2017 influenza season in the US showed that the vaccination rate among pregnant women reached 70.5% among women whose providers recommended and offered the vaccination, 43.7% when the vaccine was recommended but not offered, and 14.8% when it was neither recommended nor offered (59) (53%, 35 and 2% in our study).

In France, women must obtain a prescription from their GP or antenatal care provider, purchase the vaccine, and subsequently attend again to receive the vaccine. This process may be a significant barrier to the vaccine uptake. Several experiments are in process in France to study if getting the vaccine without prescription and injecting it at the same time in the drugstore can improve the vaccination coverage.

We found several other factors associated with increased vaccination rate but not easily modifiable by a public health program such as nulliparity (54,56), history of preterm delivery or hospital based prenatal care in their first trimester of pregnancy (54,66).

So, our study highlights the importance of incorporating education about the risk of flu and the safety/efficacy of vaccination into routine antenatal care. The pregnant women need to know that the vaccine protects them and their newborns from influenza infection and that there are very few vaccine complications for them and their babies. Our study suggests that this simple message delivered by a healthcare worker can improve the vaccination uptake.

Implications for future practice and research:

Our study suggests that in order to increase influenza vaccine compliance among pregnant women, two principal actions should guide prenatal care policies: information about influenza and its vaccine by healthcare workers and cost-free access to the vaccine. As the role of professionals appears central, it would be useful to conduct a study in order to assess their knowledge and opinions about this vaccination and to help them to improve their practice by incorporating education about influenza vaccination during their routine antenatal care.

Strengths and limitations:

On the one hand, the prospective nature of our study, the number of women included, the high participation rate (87%), and the use of a self-completed questionnaire enabled us to limit the potential for bias as much as possible. On the other hand, its single-centre nature could have induced recruitment bias, and the responses cannot be taken as representative of all pregnant women. Another limitation might be that our participants were all recruited from a university hospital, and that our sample may therefore be missing subsets of the population that tend to be more anti-vaccination or receive less education, so future studies might benefit from recruiting over a wider geographical area and from different types of sites. Finally, vaccination status was reported by the women and there is therefore potentially susceptible to reporting bias, which has been partially corrected by checking the women's medical records.

CONCLUSIONS:

Although the World Health Organization has recommended influenza vaccination for all pregnant women since 2012, only one third of the mothers in our study were vaccinated. Our study highlights that in order to increase influenza vaccination compliance among pregnant women, two principal actions should guide prenatal care policies: information about influenza and its vaccine be routinely given by healthcare workers and cost-free access to the vaccine.

Table 1: Factors associated with uptake of influenza vaccination during pregnancy according to mothers' characteristics (n=2045)

	Vaccinated		<i>p</i> [‡]
	n/N*	%	
Total	725/2045	35.5	
Age			
<25 years	97/306	31.7	0.49
≥ 25 and <30 years	230/645	35.7	
≥ 30 and <35 years	246/685	35.9	
≥ 35 years	151/408	37.0	
Educational level			
Primary	28/69	40.6	0.59
Secondary or technical	132/386	34.2	
Higher study	564/1588	35.5	
Lives with partner			
Yes	643/1803	35.7	0.56
No	81/240	33.7	
Smoked during pregnancy			
Yes	144/437	33.0	0.22
No	578/1602	36.1	
At least one comorbidity**	191/478	40.0	0.02
Respiratory	48/142	33.8	
Cardiac	28/74	37.8	
Neurological	36/93	38.7	
Nephrological	9/18	50.0	
Haematologic-immune	31/54	57.4	

Diabetes	16/30	53.3	
Chronic liver disease	10/21	47.6	
BMI \geq 40 kg/m ²	13/24	29.5	
Previous influenza vaccination			
Yes, outside pregnancy	279/548	50.9	<0.001
Yes, during a previous pregnancy	185/201	92.0	
No	249/1235	20.2	
Number of previous deliveries			
0	358/874	41.0	<0.001
1	225/704	32.0	
\geq 2	141/465	30.3	
History of preterm delivery <34 weeks			
Yes	33/76	43.4	0.14
No	691/1967	35.1	
Obstetric complications***			
Yes	288/812	35.5	0.98
No	435/1228	35.4	
Perceived frequency of influenza in the general population			
Very low to low	49/180	27.2	0.02
Intermediate	217/631	34.4	
High	452/1202	37.6	
Perceived frequency of vaccine complications in pregnant women			
Very low	352/673	52.3	<0.001
Low	154/509	30.3	
Intermediate	139/597	23.3	
High	52/141	36.9	

Perceived frequency of vaccine complications in babies

Very low	375/687	54.6	<0.001
Low	122/414	29.5	
Intermediate	128/621	20.6	
High	64/181	35.4	

Good knowledge of influenza[±]

Yes	374/606	61.7	<0.001
No	351/1439	24.4	

* Number of women vaccinated among the total number of women in the subclass

** Presence of at least one comorbidity that is an indication for influenza vaccination even outside of pregnancy according to the 2012 HAS guidelines (67)

*** Gestational diabetes, hypertension, pre-eclampsia, HELLP syndrome, infections, other (anaemia, foetal growth restriction, etc.)

¥p value was calculated by Chi 2 test

±good knowledge of influenza was defined by a knowledge score>5.4/9

Table 2: Factors associated with uptake of influenza vaccination during pregnancy according to prenatal care (n=2045)

	Vaccinated		<i>p</i> [‡]
	n/N*	%	
Total	725/2045	35.5	
Time at which prenatal care started			
First trimester	72/131	55.0	<0.001
Second trimester	410/1106	37.1	
Third trimester	241/798	30.2	
Healthcare worker providing the prenatal care			
Assistant Chief Resident	50/129	38.8	0.80
Hospital staff physician	274/734	37.3	
Hospital staff midwife	322/894	36.0	
Intern	64/187	34.2	
Healthcare worker recommending vaccination			
Gynaecologist-Obstetrician	237/467	50.7	<0.001
General practitioner	82/143	57.3	
Hospital staff midwife	229/571	40.1	
Midwife (in private practice)	25/46	54.3	
Several different professionals	76/158	48.1	
Occupational doctor, national health insurance	56/107	52.3	
Types of information received			
Recommendation for vaccination with a form for reimbursement	524/987	53.1	<0.001
Recommendation for vaccination without a form for reimbursement	176/501	35.1	
No recommendation for vaccination but reimbursement form provided	3/19	15.8	
Neither proposal for vaccination nor reimbursement form	11/507	2.2	
Vaccination recommendation			

Yes	711/1514	47.0	<0.001
No	14/528	2.7	
Receipt of a vaccine reimbursement form			
Yes	527/1006	52.4	<0.001
No	187/1008	18.6	
Sources of information about influenza vaccination (multiple responses possible)			
At least one healthcare worker	604/1378	43.8	<0.001
Not a healthcare worker**	117/611	19.1	

* Number of women vaccinated among the total number of women in the subclass

** All answers possible except healthcare workers: the media, discussion groups, family and friends, health authorities, and others

‡p value was calculated by Chi 2 test

Table 3: Women motivations to be vaccinated or not against influenza

	n	%
Motivations to be vaccinated (N=325)		
The vaccine protects me	529	73.0
The vaccine protects my baby	599	82.6
I have received sufficient information on the benefits of the vaccine	217	30.0
I am more “in favour” of vaccines in general	172	23.7
The vaccine is fully reimbursed	64	8.8
Other	23	3.2
Motivations not to be vaccinated (N=1320)		
I did not know there was a vaccine	55	4.2
I was scared for my baby’s health	317	24.0
I was scared for my health	166	12.6
I did not have enough information about the benefits and risks	422	32.0
I am rather “against” vaccines in general	350	26.5
Other	387	29.3

Table 4: Logistical regression analysis of the factors associated with influenza vaccination uptake during pregnancy in this study (n=1751)

	OR	aOR*	95 % CI**	p [‡]
Previous influenza vaccination				
No.	1	1		<0.001
Yes, not during pregnancy	4.1	4.1	3.1-5.5	
Yes, in a previous pregnancy	45.8	43.9	22.8-84.4	
Number of previous deliveries				
≥ 2	1	1		<0.001
1	1.1	1.6	1.1-2.4	
0	1.6	2.5	1.7-3.7	
History of preterm delivery <34 weeks				
No.	1	1		0.02
Yes	1.4	2.3	1.1-4.9	
Perceived frequency of vaccine complications in babies				
High	1	1		0.005
Intermediate	0.3	0.9	0.5-1.5	
Low	0.2	0.5	0.3-0.9	
Very low	0.4	1.1	0.5-2.2	
Good knowledge of influenza				
No.	1	1		<0.001
Yes	5.0	3.1	2.2-4.4	
Hospital-based prenatal care beginning				
Third trimester	1	1		0.02
Second trimester	1.4	1.2	0.9-1.6	
First trimester	2.8	2.1	1.2-3.7	
Vaccination recommendation				
No.	1	1		<0.001
Yes	32.5	18.8	10.0-35.8	
Receipt of a vaccine reimbursement form				
No.	1	1		<0.001
Yes	4.8	2.0	1.5-2.7	
Profession of the healthcare worker offering the vaccination[‡]				
Gynaecologist-Obstetrician	1	1		0.05
General practitioner	1.3	1.6	1.0-2.8	
Hospital staff midwife	0.6	0.9	0.6-1.3	
Midwife (in private practice)	1.1	2.2	0.9-5.1	
Several different professionals	0.9	1.2	0.7-1.9	
Occupational doctor, national health insurance	1.1	1.7	1.0-2.9	
Sources of information about influenza vaccination (multiple responses possible)				
No healthcare worker ***	1	1		<0.001
At least one healthcare worker	3.3	1.8	1.3-2.6	

* Adjusted odds ratio: determined by multivariate logistic regression of influenza vaccination for the variables with a p-value <0.20. The variables not significantly associated with vaccination (p>0.05) are not presented: the presence of at least one comorbidity**, perceived frequency of influenza, and perceived frequency of vaccine complications in mothers

** 95% confidence interval

*** All answers possible except healthcare workers: the media, discussion groups, family and friends, health authorities, and others

¥p value was calculated by multivariate logistic regression analyses

£ Only women who had received a vaccination recommendation were analysed (n=1300).

II. Article 2 :

Dans l'article précédent, nous avons donc montré l'**importance des connaissances des femmes enceintes** et de la **proposition de la vaccination** par les professionnels de santé comme déterminants de recours à la vaccination antigrippale. Ces résultats appuient nos hypothèses de départ.

Afin de pouvoir améliorer la couverture vaccinale antigrippale pendant la grossesse, nous nous sommes ensuite demandé comment améliorer les connaissances des femmes enceintes, ce qui nous a conduit à chercher quels étaient **les déterminants d'une bonne connaissance chez les femmes enceintes, concernant la grippe et la vaccination antigrippale pendant la grossesse.**

Nous avons repris la même étude que pour l'article précédent, ainsi que le score de bonne connaissance calculé dans l'analyse étudiée en amont (Annexe 2).

Ici aussi, le doctorant a participé à l'élaboration du score de bonne connaissance, à la méthodologie de l'article, à l'analyse de données et à la rédaction de l'article.

Determinants of pregnant women's knowledge about influenza and the influenza vaccine: a large, single-centre cohort study.

Short title: Determinants of pregnant women's knowledge about influenza and the influenza vaccine

Abstract:

Introduction: Although influenza can lead to adverse outcomes during pregnancy, the level of influenza vaccine coverage among pregnant women remains very low. According to the literature, a high level of knowledge about influenza disease and the influenza vaccine is one of the main determinants of vaccination coverage. The objective of the present study was to describe pregnant women's level of knowledge of these topics and to identify any corresponding determinants.

Material and methods: A prospective, observational, hospital-based study of women having given birth in our university medical centre during the 2014-2015 influenza season. Data were collected through a self-questionnaire or extracted from medical records. Determinants of highest knowledge were identified using logistic regression.

Results: Of the 2069 women included in the study, 827 (40%) did not know that influenza can lead to severe adverse outcomes for the mother, and 960 (46%) did not know about possible severe adverse outcomes for the baby. Two hundred and one women (9.8%) stated that the vaccine was "contraindicated" or "unnecessary" during pregnancy. Only 205 women (17%) had been vaccinated during a previous pregnancy. Determinants of the highest level of knowledge were age over 24, a high educational level, previous influenza vaccination, nulliparity, and the recommendation of vaccination by a healthcare professional.

Conclusions: Recommending vaccination during pregnancy appears to increase knowledge about influenza and its vaccine among pregnant women.

INTRODUCTION:

Seasonal influenza is a common, contagious viral illness associated with elevated risks of morbidity and mortality in pregnant women (33) – even in women with no comorbidities (49). Furthermore, a safe influenza vaccine is available; a review of 15 years of surveillance data in the United States (covering 750 million doses of influenza vaccine) did not highlight any safety problems for either the foetus or the mother (34–36). Moreover, vaccination can reduce the incidence of influenza cases among vaccinated pregnant women by 70% (27) and among their infants by 63% (44). The vaccine reduces the incidence of episodes of febrile respiratory illness by 29% (40), and maternal vaccination confers effective protection on the newborn (40). This is why the seasonal influenza vaccination of pregnant women (regardless of gestational age) is recommended by World Health Organization (33), the American College of Obstetricians and Gynecologists, and the Centers for Disease Control and Prevention (52). Despite these observations, influenza vaccination coverage among pregnant women remains very low: 7% in France (2015-2016) (47), 45% in England (2016-2017) (58), and 37% in the United States (2016-2017) (59).

Several studies have found that a good level of knowledge about influenza disease and the influenza vaccine is associated with higher rates of vaccine uptake during pregnancy (48,53,57). However, few of these studies looked for determinants of high knowledge about these topics, and all had a small sample size (68,69). The objectives of the present study were to describe pregnant women's levels of knowledge about these topics and to identify any corresponding determinants.

MATERIAL AND METHODS:

During the 2014-2015 influenza season, we conducted a prospective, observational, single-centre study in a university medical centre's level III maternity unit (Lille University Medical Centre, Lille, France). All women having received antenatal care during the 2014-2015 influenza vaccination campaign and having giving birth in our maternity unit between November 17th, 2014, and June 5th, 2015 were eligible for inclusion. All the included women gave their written, informed consent to participation. Each day, an investigator (OM or ED, both of whom are MDs in the unit) went to the unit to explain the study to the attending women and to collect their consent to participation in the study. We excluded women under the age of 18, those with a contraindication to influenza vaccination, and those who did not speak French. Some items of data were extracted from medical records. All the study participants were invited to fill out a self-questionnaire during their postpartum hospital stay (Appendices S1A and S1B).

The primary study outcome was a high level of knowledge about influenza and its vaccine, as assessed using a self-questionnaire based on that described by Yudin et al. (48). We chose Yudin et al.'s questionnaire because it has been applied in several articles in this field (53,57,69). To the best of our knowledge, none of the questionnaires used to probe levels of knowledge about vaccination has been psychometrically validated. Our questionnaire was drafted by a multidisciplinary expert group that included obstetricians, infectious disease specialists, general practitioners, and statisticians. We first tested the questionnaire on a randomly selected group of 10 pregnant women receiving antenatal care. Two questions were modified after this test. The questions covered the frequency of influenza infection,

serious complications of influenza for mothers and infants, the frequency of complications of vaccination among mothers and their infants, and guidelines about vaccination during pregnancy. Before the study, we worked with the multidisciplinary expert group to create a "knowledge score" about influenza and its vaccine, based on the answers to 10 questions in the self-questionnaire. Each expert attributed a score of 0, 0.5 or 1 for each possible answer. The final scores for each answer were then decided on by consensus, and adopted as the scoring system. Depending on the type of question, the women were invited to answer "yes" or "no", to check an answer, or to circle a number (from 0 to 9) that corresponded to their opinion. For example, the answers to the question "In your opinion, the influenza vaccine causes complications for the baby" ranged from very rarely (0) to very frequently (9). A point was awarded for an answer below 3; no points were awarded for an answer of 3 or above (Appendix S2). The overall score ranged from 0 to 10 points, a woman was considered to have a high level of knowledge if she achieved a score in the fourth quartile of the distribution (more than 6.0 out of 10, in the present study).

The following variables were considered as possible determinants of a high level of knowledge: the mother's sociodemographic characteristics (age, educational level, and living with a partner or not); the mother's medical history before pregnancy (pre-existing comorbidities for which influenza vaccination is recommended by the French guidelines (67), having being vaccinated against influenza prior to the current pregnancy, the number of previous deliveries, and any history of preterm delivery (before 34 weeks of gestation)); the characteristics of the current pregnancy (smoking status, and obstetrical complications such as gestational diabetes, gestational hypertension, pre-eclampsia, HELLP syndrome, infections, and foetal growth restriction); prenatal care (the healthcare professional providing the prenatal

care: a gynaecologist/obstetrician, a general practitioner, a hospital midwife, or a private midwife), and the profession of the healthcare professional who recommended vaccination (i.e. the source of information about the vaccine).

Data on prenatal care and on the mother's knowledge about influenza and its vaccine were extracted from the self-questionnaire. Data on the mother's sociodemographic characteristics, the mother's medical characteristics before pregnancy, and the current pregnancy's characteristics were extracted from medical records.

Statistical analyses:

Determinants associated with a high level of knowledge were identified in bivariate and multivariate analyses. Variables significantly associated with a high level of knowledge in the bivariate analysis ($p < 0.20$) were included in the multivariate model. Percentages were compared in a chi-squared test or (depending on the number of individuals) Fisher's exact test. We calculated adjusted odds ratios (aORs) with their 95% confidence interval (CI). The threshold for statistical significance was set to $p < 0.05$. All statistical analyses were performed with STATA software (version 13.0.0, StataCorp LP, College Station, TX, USA).

Ethical approval: The study's objectives and procedures were approved by the local independent ethics committee (CEROG, Lille, France; reference: OBS 2014-11-01).

RESULTS

Of the 2862 women having giving birth during the study period, 370 (12.9%) did not receive the study questionnaire because the investigator did not attend the maternity unit during the women's stay, and 138 (5.5%) were excluded (Figure 1). Next, 69 of the 2358 eligible women (2.9%) refused to participate, and 216 (9.2%) did not return the study questionnaire. Hence, 2069 women of the 2354 eligible women were included in the study (87.9%).

Our data on the women's knowledge about influenza disease and the influenza vaccine are summarized in Table 1. Firstly, 827 of the women (40.1%) did not know that influenza can lead to serious complications for the mother, and 960 (46.6%) did not know that influenza can lead to be serious complications for the baby. Secondly, 201 women (9.8%) considered the vaccine to be "contraindicated" or "unnecessary" during pregnancy. Only 205 women (17.4%) had been vaccinated during a previous pregnancy. 1391 women (69.2%) listed a healthcare professional as their main source of information. 870 (45.7%) of the women estimated that the frequency of adverse reactions to the influenza vaccine was "common" or "very common" for mothers, and 906 (48.0%) estimated that the frequency of adverse reactions to the vaccine was "common" or "very common" for babies. The distribution of the knowledge score data is shown in Figure 2. The median score [interquartile range] was 4.5 [3.5-6.0]). A total of 608 women (29.4%) had the highest level of knowledge (i.e. a knowledge score in the fourth quartile, corresponding to 6 and over).

Table1: Women's level of knowledge about influenza and its vaccine during pregnancy

	n	%
Perceived frequency of influenza in the general population (n=2020)†		
Very rare (0 – 2) *	79	3.9
Rare (3 – 4) *	353	17.5
Common (5 – 6)	1124	55.6
Very common (7 – 9)	464	23.0
Influenza can induce serious complications for the mother (n=2060)		
Yes*	1233	59.9
No.	147	7.1
I don't know	680	33.0
Influenza can induce serious complications for the baby (n=2062)		
Yes*	1102	53.4
No.	134	6.5
I don't know	826	40.1
Utility of influenza vaccination during pregnancy (n=2055)		
Contraindicated	107	5.2
Unnecessary	94	4.6
Might be useful *	875	42.6
Definitely useful*	979	47.6
Recommendation of vaccination during pregnancy (n=2064)		
Either not obligatory or not recommended	247	12.0
Obligatory *	60	2.9
Recommended *	1525	73.9
I don't know	232	11.2
Previous influenza vaccination (n=2065)		
No	1245	60.3
Yes, outside pregnancy	554	26.8
Yes, during a previous pregnancy (17.4% of the 1180 multiparous women)	205	9.9
I don't know	61	3.0
Sources of information about influenza vaccination (each source could be named on the questionnaire) (n=2010)		
Healthcare professionals (as well as other sources, potentially) ^a	1391	69.2
Other sources only (i.e. not healthcare professionals) ^b	619	30.8
Perceived frequency of adverse reactions to the vaccine among mothers (n=1902) †		
Very rare (0 – 2)*	525	27.6
Rare (3 –4)	507	26.7

Common (5 – 6)	706	37.1
Very common (7 – 9)	164	8.6
Perceived frequency of adverse reactions to the vaccine among babies		
(n=1887) ‡		
Very rare (0 – 2)*	531	28.1
Rare (3 – 4)	420	22.3
Common (5 – 6)	664	35.2
Very common (7 – 9)	242	12.8

* considered to be a correct answer by the expert group

‡ the responses are adapted from a number scale from 0 to 9.

^a Either healthcare professionals only, or healthcare professionals and other sources, such as the media, discussion groups, family & friends, health authorities, etc.

^b All possible sources (the media, discussion groups, family & friends, health authorities, etc.) other than healthcare professionals.

In the bivariate analysis, the factors associated with the highest level of knowledge were older maternal age, non-smoking status, previous influenza vaccination, a low number of children, prenatal care provided by an obstetrician in hospital, a recommendation of vaccination by a healthcare professional, and having received information from one or more healthcare professionals (Table 2).

Table 2: Factors associated with the highest level of knowledge among women about influenza and its vaccine during pregnancy: a bivariate analysis

	n/N*	%	p
Total	608/2069	29.4	
Age (years)			<0.001
≤ 24	62/314	19.7	
25 - 29	195/653	29.9	
30 - 35	220/689	31.9	
≥35	131/412	31.8	
Educational level			<0.001
Primary education	11/73	15.1	
Secondary or technical education	71/394	18.0	
Higher education	525/1600	32.8	
Living with a partner			0.006
Yes	554/1820	30.4	
No	54/247	21.9	
Smoked during pregnancy			0.007
Yes	108/444	24.3	
No	500/1619	30.9	
Number of previous deliveries			0.002
0	283/887	31.9	
1	217/711	30.5	
≥ 2	108/469	23.0	
History of preterm delivery (<34 weeks)			0.35
Yes	19/77	24.7	
No	589/1990	29.6	
Pre-existing comorbidities for which influenza vaccination is recommended			0.60
Yes	147/485	30.3	
No	457/1573	29.1	
Previous influenza vaccination			<0.001
Yes, outside pregnancy	231/554	41.7	
Yes, during a previous pregnancy	92/205	44.9	
No	271/1245	21.8	
Obstetric complications^a			0.13
Yes	227/822	27.6	
No	381/1242	30.7	
Healthcare professional providing prenatal care			0.26

Hospital staff midwife	257/904	28.4	
Hospital staff physician	243/741	32.8	
Assistant chief resident	37/130	28.5	
Intern	54/187	28.9	
Vaccination recommended by a healthcare professional			<0.001
Yes	522/1522	34.3	
No	86/531	16.2	
Healthcare professional recommending vaccination			0.002
Hospital staff midwife	165/584	28.2	
Private midwife	26/66	39.4	
General practitioner	80/202	39.6	
Gynaecologist/obstetrician	214/576	37.2	
Sources of information (each source could be named on the questionnaire)			<0.001
Healthcare professionals (as well as other sources, potentially) ^b	450/1391	32.4	
Other sources only (not healthcare professionals) ^c	151/619	24.4	

^a The proportion of women with the highest level of knowledge in each subgroup; n: the number of women with the highest level of knowledge in the subgroup; N: the total number of women in the subgroup.

^a *Gestational diabetes, gestational hypertension, pre-eclampsia, HELLP syndrome, infections, or another reason.*

^b Either healthcare professionals only, or healthcare professionals and other sources, such as the media, discussion groups, family & friends, health authorities, etc.

^c All possible sources (the media, discussion groups, family & friends, health authorities, etc.) other than healthcare professionals.

In the multivariate logistic regression analysis (Table 3), the variables significantly associated with the highest level of knowledge about influenza and its vaccine were age over 24, a high educational level, previous influenza vaccination, nulliparity, and a recommendation of vaccination by a healthcare professional.

Table 3: Factors associated with women's knowledge about influenza and its vaccine during pregnancy: a multivariate analysis (N=1983)

	aOR ^a	95%CI ^b	p
Age (years)			0.02
≤ 24	1		
25 - 29	1.52	1.1-2.2	
30 - 35	1.80	1.2-2.6	
≥35	1.76	1.2-2.7	
Educational level			<0.001
Primary education	1		
Secondary or technical education	1.3	0.6-2.7	
Higher education	2.3	1.1-4.7	
Number of previous deliveries			0.006
≥2	1		
1	1.5	1.1-2.0	
0	1.6	1.2-2.2	
Previous influenza vaccination			<0.001
No	1		
Yes, outside pregnancy	2.5	2.0-3.1	
Yes, during a previous pregnancy	2.9	2.1-4.0	
Vaccination recommended by a healthcare professional			<0.001
No	1		
Yes	2.4	1.8-3.1	

^a The adjusted odds ratio for a high level of knowledge about influenza and its vaccine, determined in a multivariate logistic regression analysis. Variables not significantly associated ($p>0.05$) with knowledge about influenza and its vaccine (living with a partner, smoking during pregnancy, obstetric complications, and sources of information) are not presented.

^b CI: confidence interval.

Discussion

Our results show that a large proportion of pregnant women having given birth in a university medical centre in France were not sufficiently knowledgeable about influenza and its vaccine. Indeed, about half of the pregnant women did not know that influenza can lead to serious complications for them and/or for their babies. With a view to improving vaccine coverage in this population, the only easily actionable factor associated with a higher level of knowledge about influenza and its vaccine was the recommendation of vaccination during pregnancy by a healthcare professional.

Our research was observational and so was affected by the inherent limitations of this type of study. Furthermore, the study was carried out during the 2014-2015 influenza season; in the middle of the vaccination campaign, the vaccine's efficacy was challenged in the French media. This may have influenced the vaccination rate and/or the women's answers in the questionnaire.

Although the women's level of knowledge was far from optimal, we found that the vaccination rate among the study participants was 35%; this value is higher than the national average for France (7%, currently) (47) but is similar to the rates observed in other countries: 45% in England in 2017 (58) and 37% in the United States in 2017, for example (59). However, we did our best to reduce the risk of bias: our prospective study included a high proportion (87.1%) of the women who gave birth in our hospital during the study period, and the questionnaire response rate was high (87.9%). Moreover, we chose to administer a self-questionnaire so that the participants' answers were not influenced by the medical staff.

In the present study, a high level of knowledge about influenza and its vaccine was defined as knowing that influenza infection (i) is frequent and contagious, (ii) can lead to rare but serious complications for pregnant women and babies, and (iii) can be mitigated by a readily available, effective, guideline-recommended vaccine. We found that 40.1% of the pregnant women did not know that influenza could cause serious complications for the mother, and 46.6% did not know that influenza could cause serious complications for the baby. These values of over 40% were higher than those reported in the United States (55), Switzerland (57) and Korea (53), where prospective studies found that only 20% of women did not know that influenza could have serious complications during pregnancy for the mother and her baby.

In the present study, the majority of the participants (90.2%) believed that the vaccine “might be useful” or “definitely useful”. Our results differed from those observed in an Italian study, in which only 41% of pregnant women thought that a vaccine could protect pregnant women against influenza (68). The same result was found in the French Vaccinoscopie® study in 2014; only a third of the 300 surveyed women with a child aged 12 months or younger thought that it was “rather important” or “very important” to be protected against influenza during pregnancy (70). The vaccine’s perceived utility might be counterbalanced by a fear of adverse reactions (62). In the literature, 30% to 50% of pregnant women thought that the vaccine might induce influenza or influenza-like symptoms (71), and 15% feared that the vaccine could cause foetal defects (72) or premature birth (53). More generally, 46% of the women in the US study considered that vaccination during pregnancy was not safe (55).

Although higher vaccination rates are generally found among women with a better level knowledge about influenza and its vaccine (53,57,69,71,73), the present study is one of the few to have looked for factors associated with a high level of knowledge

(55,68,69). In a study in Saudi Arabia, Mayet et al. interviewed 998 women about the influenza vaccine; working women and those with at least one child had a higher level of knowledge (69). Napolitano et al.'s study of 372 pregnant women in Italy found that a better level of knowledge was associated with older age, a higher educational level, and a high-risk pregnancy (68). In the present study, we found that age over 24, a high educational level, previous influenza vaccination, nulliparity, and having been recommended influenza vaccination during pregnancy were significantly associated with greater knowledge about influenza and its vaccine. Unsurprisingly, Mayet et al. and Napolitano et al. also found that a higher educational level was associated with a higher level of knowledge about influenza (68,69). Furthermore, women having been previously vaccinated against influenza have the highest level of knowledge about influenza and its vaccine. This is also true outside pregnancy (57,71,74).

Among the factors found here to be associated with the highest level of knowledge about influenza and its vaccine among pregnant women, the recommendation of vaccination during pregnancy is the only one that could be promoted by a public health initiative. We are not aware of a study that has evaluated the specific impact of recommending vaccination on a woman's level of knowledge during pregnancy. However, several studies have evidenced a direct, statistically significant association between a recommendation of vaccination and subsequent vaccination (57,71). In the present study, influenza vaccination had been recommended to 73.6% of the participants. Only a third of these women had a high level of knowledge, even though 67.2% of the study population reported that healthcare professionals constituted their main source of information about influenza and its vaccine. Similarly, 65% of American women considered healthcare professionals to be the most important,

trusted source of information during their pregnancy (75). Hence, it seems possible that the suboptimal level of knowledge in our study population might be due to a lack of knowledge among healthcare professionals – some of whom may not be convinced of the value of vaccination against influenza. Indeed, awareness of an elevated risk of influenza-induced deaths among pregnant women was heightened by the H1N1 influenza pandemic in 2009 (76). Moreover, scepticism about vaccination among healthcare professionals in France has notably increased since the 1990s (77).

On the basis of our present results, recommending vaccination during pregnancy appears to increase knowledge about influenza and its vaccine among pregnant women. An evaluation of healthcare providers' knowledge and attitudes regarding influenza vaccination is warranted.

Acknowledgments: We thank Philippe Dufour, Sophie Vanderstichele, Marielle Roumilhac and Yamina Hammou for their help with inclusion of the study participants.

III. Article 3 :

Dans les deux articles précédents, nous avons montré **le rôle crucial du professionnel de santé dans le recours à la vaccination antigrippale chez la femme enceinte**. Dans le premier écrit, nous avons en effet révélé que la proposition vaccinale par un professionnel de santé était un déterminant majeur du recours à la vaccination. Dans le second, nous avons là aussi montré que la proposition vaccinale par un professionnel de santé s'accompagnait d'une meilleure connaissance par les femmes de la grippe et de la vaccination antigrippale pendant la grossesse, elles-mêmes liées à des chances plus élevées de vaccination.

Dans ces conditions, nous avons bâti une **seconde étude ad hoc**, destinée à explorer les connaissances, les pratiques et les freins à la vaccination antigrippale chez les professionnels de santé prenant en charge des femmes enceintes au sein du réseau périnatal OMBREL (Organisation Mamans Bébé de la Région Lilloise). Ce réseau est constitué de 7 maternités, parmi lesquelles se trouvait la maternité universitaire dont il s'est agi dans la première étude.

Pour les besoins de cette étude, le groupe d'expert multidisciplinaire qui avait créé le questionnaire pour l'étude auprès des femmes enceintes s'est attaché à créer un **nouveau questionnaire**, destiné cette fois aux professionnels de santé (Annexe 3). Les questions portaient d'une part sur les connaissances des professionnels de santé quant à la grippe et ses conséquences potentielles pour la mère et le fœtus ; ainsi que sur le vaccin antigrippal, ses bénéfices et ses effets indésirables. Elles concernaient d'autre part leurs pratiques, les obstacles qu'ils rencontrent avec la vaccination antigrippale et leurs sources d'information. Afin d'obtenir le meilleur taux de réponse possible et de s'adapter aux organisations, celui-ci a été proposé par

courrier pour 6 des 7 maternités du réseau de périnatalité (une maternité de niveau 3, quatre de niveau 2, une de niveau 1). Pour la maternité de niveau 2 restante ainsi que pour les praticiens libéraux du réseau, l'auto-questionnaire a été proposé par mail. En cas de non réponse à l'auto-questionnaire, deux relances ont été effectuées.

Le doctorant a participé à l'élaboration du questionnaire, à la méthodologie de l'étude, au data management, à l'analyse des données et à la rédaction de l'article.

Knowledge, practices and barriers reported by healthcare professionals with regard to influenza vaccination during pregnancy.

Highlights: Greater knowledge among professionals is not linked to practices that encourage vaccination.

ABSTRACT

Context: Although influenza vaccination is recommended for pregnant women, the vaccine coverage rate remains very low worldwide.

Objective: To evaluate knowledge, practices and barriers reported by healthcare professionals with regard to influenza vaccination during pregnancy.

Method: We performed a prospective, observational, self-questionnaire-based study of healthcare professionals in a mother & child health network just before the 2014/2015 influenza vaccination campaign. The objective was to identify knowledge, practices and barriers reported by healthcare professionals with regard to influenza and influenza vaccination during pregnancy.

Results: 144 of the 350 of the invited healthcare professionals (41%) replied to the survey. 89 of the 144 respondents (62%) knew that influenza during pregnancy increases the mother's risk of death by a factor of five. 138 (97%) were familiar with the guidelines on vaccination during pregnancy, and 99 (70%) recommended vaccination to their patients "often or very often". 102 (71%) stated that they had been vaccinated in the previous two years, and 76 (53%) were aware that they could give the patient a form for full reimbursement of the vaccine. The main reported barriers to vaccination were refusal by the patient (54%), the healthcare professional's admitted lack of knowledge about influenza and the influenza vaccine (32%), and a lack of time (20%). 36 (25%) had a good level of knowledge about influenza and the influenza vaccine; however, this was not associated with practices that encouraged vaccination.

Conclusion: Even though the surveyed healthcare professionals stated clearly that a lack of knowledge about influenza and the influenza vaccine was a barrier, a good level of knowledge was not associated with practices that encouraged vaccination.

Key words: influenza vaccination, pregnancy, healthcare professional, knowledge

INTRODUCTION

The viral disease influenza can be lethal – especially in at-risk populations, such as pregnant women (33,78). During the 2009 influenza pandemic, pregnant women had a 4- to 5-fold greater risk of severe influenza than other adults of the same age and accounted for 4 to 13% of the influenza-related deaths (79).

The influenza vaccine confers effective protection against the disease, with a 70% reduction in the incidence of influenza among vaccinated mothers (27) and (thanks to the maternal transmission of antibodies) among their babies up to the age of 6 months (42). In the United States, an analysis of 15 years of monitoring data on 750 million vaccinations did not reveal any safety problems for the foetus or the mother (34). These findings prompted the World Health Organization (WHO) to recommend influenza vaccination for all pregnant women, regardless of the trimester of pregnancy (33).

However, vaccine coverage among pregnant women remains low; it was 7% in France in 2016 (47). The coverage rates measured in other developed countries are barely higher; according to a study performed in 2018 by the European Centre for Disease Prevention (ECDC), the vaccine coverage rate in Europe ranged from 0.5% to 58.6% (80). Healthcare professionals have a key role in the uptake of influenza vaccination. In fact, some researchers have highlighted the importance of a recommendation of vaccination by a healthcare professional and have suggested that this is the most important determinant of uptake by pregnant women (64,81,82).

The primary objective of the present study was to determine the reasons for the low vaccine coverage rate in France. To this end, we evaluated knowledge, practices and barriers reported by healthcare professionals with regard to influenza and influenza vaccination during pregnancy.

MATERIALS AND METHODS

We performed a prospective, observational, multicentre study from August 31st to October 1st, 2014. The study population comprised healthcare professionals working in or collaborating with 7 maternity units in and around the city of Lille (France). These healthcare professionals included hospital-based and/or private-practice gynaecologists-obstetricians, general practitioners, and midwives. All respondents gave their consent to participation in the study.

The healthcare professionals' data were collected via a self-questionnaire (Supplementary Material). In order to obtain the best possible response rate and adapt the study to the maternity units' organisational procedures, the self-questionnaire was posted to six of the seven units (one level 3 unit with a neonatal intensive care unit, four level 2 units without a neonatal intensive care, and one level 1 unit without a neonatal care unit) and e-mailed to the remaining unit (a level 2 unit) and the network's private-practice physicians. The questionnaire covered (i) the healthcare professionals' knowledge of (i) influenza and its potential impact on the mother and the foetus, (ii) the perceived nature, benefits and side effects of the influenza vaccine, (iii) the healthcare professionals' practices with regard to the vaccine, (iv) the barriers that they encountered, and (v) their sources of information. The questionnaire was developed by a multidisciplinary committee of experts: infectious disease specialists, epidemiologists, gynaecologist-obstetricians, midwives, and statisticians, and had been tested in a pilot phase. If healthcare professionals failed to reply to the self-questionnaire, they were chased up twice by e-mail.

In order to evaluate the healthcare professionals' knowledge about influenza and vaccination during pregnancy, a "knowledge score" had been developed prior to the study by the same group of experts. The score was based on nine of the self-questionnaire's items dealing with the epidemiology of influenza infection, influenza vaccination, the indications of vaccination, and the risks outside and during pregnancy. Arbitrarily, the group of experts set the threshold for a "good" level knowledge to 80%, i.e. a score of least 7.2 out of 9. All statistical analyses were performed with STATA software (version 13.0.0, StataCorp LP, College Station, TX, USA). Percentages were compared using a chi-squared test or Fisher's test, depending on the sample size. The threshold for statistical significance was set to $p < 0.05$. The study's objectives and procedures were approved by the local independent ethics committee (CEROG, Lille, France; reference: OBS 2014-11-01).

RESULTS

Of the 340 questionnaires sent out, 144 were returned (41%). With regard to the healthcare professionals' knowledge about influenza (Table 1), most respondents knew that influenza is a highly contagious disease, about two thirds knew that influenza during pregnancy increases the mother's risk of death by a factor of five, and over nine in ten knew that the vaccination against influenza is recommended regardless of the trimester of pregnancy. With regard to the influenza vaccine, more than eight in ten healthcare professionals considered that it provides strong protection against illness, three quarters knew that it is not a live vaccine, and over two thirds reported that they had been vaccinated in the two years preceding the survey. Moreover, the majority of the healthcare professionals considered that the vaccine was associated with very few side effects. However, only 8% of the respondents stated that serious complications were possible but rare, and nearly all considered that the adverse foetal events were not serious and not frequent.

With regard to the healthcare professionals' practices (Table 2), over two thirds of the respondents stated that they recommended influenza vaccination to their pregnant patients "often or very often", and 80% considered vaccination for themselves or their spouse. However, half did not know about the reimbursement form provided by the French social security system, and only a third of those who were aware of the reimbursement form actually handed it over to their patients. Moreover, the majority of healthcare professionals reported barriers to influenza vaccination. The most frequently cited barriers were refusal by the pregnant women (mentioned by 54% of the healthcare professionals), their own lack of medical knowledge about influenza

and the influenza vaccine (33%), and a lack of time (21%). Lastly, the healthcare professionals' main sources of information were official sources (the French Ministry of Health, the French Medicines Agency, other official regulatory and advisory bodies, regional health agencies, etc.) (63%) and colleagues/team meetings (52%).

The data on practices reported by the healthcare professionals with vs. without a good level of knowledge about influenza are summarized in Table 3. It shows that the healthcare professionals who had a good influenza knowledge were not more likely to have been vaccinated against influenza in the previous two years, did not give more forms of vaccine reimbursement, and were not more likely to recommend the influenza vaccine to patients or consider it for themselves or their partner in the event of pregnancy.

DISCUSSION

Our study of healthcare professionals managing with pregnant women showed that the main barrier to vaccination against influenza was refusal by the patient, followed by the healthcare professional's own lack of knowledge. However, we found that a good level of knowledge among healthcare professionals was not associated with practices that encouraged vaccination.

Our study had several strengths, including its prospective design and a study population that encompassed both private-practice and hospital-based healthcare professionals. Furthermore, the use of a self-questionnaire probably reduced bias in the respondents' answers. However, the study also had some limitations. Firstly, the response rate was low; it might be that the respondents felt more concerned by the subject and/or were more committed to preventing influenza. Secondly, the self-reported study data may not have corresponded to the respondents' actual practices. However, these limitations affect all studies with this type of design.

Seventy percent of the surveyed healthcare professionals stated that they had been vaccinated against influenza in the previous two years; this is a satisfactory vaccination rate. In fact, a study performed by the ECDC in 2018 found that vaccination rates ranged from 15.6% to 63.2% (median: 30.2%) (80). With regard to the healthcare professionals' knowledge, our results showed that the great majority were aware of the WHO guidelines on influenza vaccination during pregnancy (33).

With regard to practices, 70% of the surveyed healthcare professionals stated that they suggested vaccination to pregnant women “often or very often”. A 2020 literature review found vaccine recommendation rates below 50% in about a third of the studies of this topic (83). Our finding is in line with a French study published in 2014, in which nine out of ten women stated that they had not received enough information about influenza vaccination during pregnancy (70). Similarly, in a study of non-vaccinated pregnant women in the United States, 83% of the respondents considered that the information provided by their physician was not enough to convince them about a vaccination that they would readily have accepted if better informed (81).

Our study highlighted a number of barriers to influenza vaccination during pregnancy. The barriers most frequently mentioned by the healthcare professionals were refusal by the patient and their own lack of knowledge concerning influenza and the influenza vaccine. Refusal by the patient was also identified in a 2012 study of 416 pregnant women, most of whom did not get vaccinated (84). The main reasons mentioned by the women were the fear of vaccine side effects and the feeling of not being at risk of complications (53,54,57,70,84). With regard to the lack of knowledge mentioned by the healthcare professionals in our study, the same type of result was found in a 2009 study in the United States; only 46% of the obstetric healthcare workers knew how to identify the symptoms of influenza in a pregnant woman, and the majority stated that they lacked knowledge about influenza and the influenza vaccine (85). These results were confirmed by a literature review in which a lack of knowledge was one of the most frequently encountered barriers to vaccination (83).

Our study also highlighted an apparent dissociation between the healthcare professionals' level of knowledge about influenza and their reported practices. In fact, healthcare professionals with a good level of knowledge (i) were not more likely to be vaccinated against influenza, (ii) did not provide the patient with a vaccine reimbursement form more frequently, (iii) were not more likely to recommend influenza vaccination, and (iv) did not intend to get vaccinated (or recommend vaccination) if they (or their spouse) were to become pregnant. This dissociation between knowledge and practice can affect all the areas in which beliefs have a role, and vaccination in particular (86,87). Furthermore, this dissociation was also found in a literature review of barriers to the recommendation of vaccination by healthcare professionals (83).

The dissociation between knowledge and attitudes found in the present study might be due (at least in part) to underestimation of the risk associated with the disease, a fear of hidden side effects, and/or unavowed conflicts of interest (83,87). Firstly, it seems that support for vaccination is related to the perceived seriousness of the disease, which can be underestimated for influenza (88). In a qualitative study of 17 general practitioners in Australia, most perceived the risk of severe influenza during pregnancy to be low (89). Others were aware that pregnancy was a risk factor for severe influenza but had never been confronted with this situation in their practice; hence, they tended to underestimate the risk. Many also considered (wrongly) that pregnant women with a comorbidity were the only ones at risk of severe influenza (89). Secondly, a certain number of fears and/or false beliefs about the vaccine might limit its use. In a 2009 study performed in the United States, a third of the healthcare professionals stated that they did not comply with the vaccine guidelines and 65% of

them even considered that the vaccine influenza was potentially dangerous during pregnancy (85).

Lastly, our study indicated that a good level of knowledge of influenza and the influenza vaccine among healthcare professionals was not associated with practices that encouraged vaccination. The reasons for this lack of an association are not clear and thus require additional investigation. Under-estimation of the risk of severe influenza or the fear of an adverse reaction to the vaccine are possible explanations; if this is the case, it is probably by acting on the healthcare professionals' behavioural determinants that we will be able to significantly increase the influenza vaccine coverage rate during pregnancy.

Table 1: Healthcare professionals' knowledge and perceptions of influenza and the influenza vaccine during pregnancy, n=144

	N (%)
Contagiousness of influenza (n=143)	
Very low	3 (2.1)
Low	0 (0.0)
Moderate	13 (9.1)
High *	127 (88.8)
Relative increase in the risk of death for a pregnant woman with influenza (n=142)	
Zero	0 (0)
Five-fold *	88 (61.9)
Fifteen-fold	18 (12.7)
Does not know	36 (25.4)
Recommendation of vaccination in pregnancy (n=143)	
No	0 (0)
Yes, during the first trimester only	2 (1.4)
Yes, during the second trimester only	2 (1.4)
Yes, during the third trimester only	1 (0.7)
Yes, during any trimester *	138 (96.5)
Degree of protection provided by the influenza vaccine (n=141)	
Very low	0 (0.0)
Low	1 (0.7)
Moderate	23 (16.3)
High *	117 (83.0)
Live vaccine, yes or no (n=140)	
No *	109 (77.8)
Yes	12 (8.6)
Does not know	19 (13.6)
Have you been vaccinated against influenza in the previous two years? (n=143)	

Yes	102 (71.3)
Frequency and seriousness of the influenza vaccine's side effects on the pregnant woman (n=143)	
Not serious and not frequent	86 (60.1)
Serious and not frequent *	12 (8.4)
Not serious but frequent *	44 (30.8)
Serious and frequent	1 (0.7)
Frequency and seriousness of the influenza vaccine side effects on the foetus (n=137)	
Not serious and not frequent *	130 (94.9)
Serious and not frequent	6 (4.4)
Not serious but frequent	1 (0.7)
Serious and frequent	0 (0)

*: indicates the correct answer(s)

**Table 2: Practices and perceived barriers to influenza vaccination
during pregnancy (n=144)**

	N (%)
How often do you suggest influenza vaccination to pregnant women?(n=142)	
Very rarely	26 (18.3)
Rarely	17 (12.0)
Often	26 (18.3)
Very often	74 (51.4)
Would you have or recommend the influenza vaccine if you (or your partner) were pregnant? (n=142)	
No	28 (19.7)
Yes	114 (80.3)
Do you give the patient the social security reimbursement form? (n=142)	
No	30 (21.1)
Yes	46 (32.4)
I am not aware of the form	66 (46.5)
How often do you encounter barriers to influenza vaccination? (n=131)	
Very rarely	23 (17.6)
Rarely	28 (21.4)
Often	59 (45.0)
Very often	21 (16.0)
What barriers do you encounter with regard to influenza vaccination during pregnancy? ** (n=137)	
Frequent refusal by the patient	74 (54.0)
Lack of information/knowledge	45 (32.8)
Lack of time	29 (21.2)
Poor risk/benefit ratio	11 (8.0)
Non-compliance with the guidelines	6 (4.4)
What are your sources of information about influenza? ** (n=141)	
Official sources	89 (63.1)
Colleagues/team meetings	74 (52.5)
The media	16 (11.3)

(**) You can give more than one answer, if you wish

Table 3: Practices according to the level of knowledge (good vs. not good) of influenza and influenza vaccination (n=144)

	Knowledge score ≥80%		p
	No n (%)	Yes n (%)	
How often do you suggest influenza vaccination to pregnant women in the pregnant woman? Often/Very often	64 (70)	24 (75)	0.56
Do you give the patient the social security reimbursement form? Yes	30 (33)	11 (34)	0.85
Have you been vaccinated against influenza in the previous two years? Yes	66 (71)	24 (75)	0.66
Would you have (or recommend) the influenza vaccine if you (or your partner) were pregnant? Yes	75 (81)	26 (81)	0.94

Discussion générale :

Dans notre étude menée chez les femmes enceintes venant d'accoucher dans une maternité universitaire pendant une saison hivernale, la couverture vaccinale a été mesurée à 35%. Les facteurs liés à un taux plus élevé de recours à la vaccination antigrippale étaient l'existence d'un antécédent de vaccination antigrippale, le fait d'être nullipare, la perception du risque de complications liées au vaccin comme « très faible » ; mais également une bonne connaissance des femmes concernant la grippe et la vaccination antigrippale, l'existence d'une proposition vaccinale par un professionnel de santé, la réception d'un formulaire de remboursement du vaccin et le fait d'avoir été informée par au moins un professionnel de santé durant la grossesse. Ces résultats nous ont amené à identifier deux voies pour tenter d'améliorer la couverture vaccinale :

1. Etablir les déterminants d'une bonne connaissance des femmes enceintes concernant la grippe et la vaccination antigrippale.
2. Chez les professionnels de santé, étudier leurs connaissances concernant la grippe et la vaccination antigrippale, ainsi que les pratiques et les freins concernant cette vaccination.

Nous avons identifié comme déterminants d'une bonne connaissance des femmes enceintes les éléments suivants : avoir un haut niveau d'éducation, de ne pas avoir moins de 24 ans, être nullipare, avoir été vaccinée contre la grippe par le passé et avoir reçu une proposition vaccinale par un professionnel de santé. Ces résultats nous ont révélé une nouvelle fois l'importance des professionnels de santé dans le recours à la vaccination antigrippale, puisque le fait d'avoir reçu une proposition

vaccinale augmentait les connaissances des femmes, elles-mêmes facteurs liés à une augmentation du recours à la vaccination.

Nous nous sommes ensuite intéressés aux pratiques et aux connaissances des professionnels de santé concernant la vaccination antigrippale chez la femme enceinte. Les professionnels de santé que nous avons interrogés avaient relativement de bonnes connaissances; bien qu'environ un quart d'entre eux ignoraient que la grippe augmente le risque de mortalité chez la femme enceinte. De la même façon, environ un tiers proposaient rarement ou très rarement la vaccination aux femmes enceintes et la moitié d'entre eux n'avaient pas connaissance de l'existence d'un formulaire de remboursement. Les principales barrières que rencontraient les professionnels de santé étaient le refus des patientes dans à peu près la moitié des cas, un manque de leurs propres connaissances dans un tiers des cas et un manque de temps dans environ un quart des cas.

Le taux de vaccination de 35% retrouvé dans notre étude est largement supérieur à celui de 7 % retrouvé au même moment chez les femmes enceintes interrogées dans le cadre de l'enquête nationale périnatale française de 2016 (47). Il était en revanche comparable avec ceux observés à la même époque en Angleterre (38,5%)(90) et aux États-Unis (37,1%) (91). Il est probable que cette différence entre le taux de 35 % observé dans notre étude et le faible taux de 7 % mesuré au niveau national soit en rapport avec la motivation conjointe des responsables médicaux de la maternité et de celle des équipes du centre hospitalier dans lequel a eu lieu notre étude, avec des actions de sensibilisation menées chaque année auprès du personnel et des femmes enceintes.

Parmi les facteurs déterminants du recours à la vaccination antigrippale, certains ne permettaient pas d'être envisagés comme des leviers d'action. C'est le cas de la nulliparité (54,56,92,93), un antécédent d'accouchement prématuré ou le suivi à l'hôpital dès le premier trimestre (54,66). Comme d'autres en revanche, nous avons mis en évidence le fait que la perception des femmes vis-à-vis de la grippe, son vaccin et ses potentielles complications étaient des facteurs influençant fortement le recours à la vaccination (48,53,54,57,62,94,95) ; tout comme une bonne connaissance de la grippe et de la vaccination antigrippale et qu'il pourrait être possible de les modifier.

Dans ces conditions, nous nous sommes spécifiquement intéressés aux connaissances des femmes enceintes, qui apparaissaient liées de façon importante au recours à la vaccination, ainsi susceptibles de faire « levier » pour augmenter le recours à la vaccination. Nous avons observé que 40% des femmes de notre étude ignoraient que la grippe pouvait entraîner des complications graves pour la mère. Ce taux est supérieur à celui retrouvé dans d'autres pays, se situant aux alentours de 20 % (53,55,57). Nous avons ensuite identifié comme facteurs augmentant ces connaissances un haut niveau d'éducation, un âge supérieur à 24 ans, un antécédent de vaccination contre la grippe, une nulliparité, ainsi que le fait d'avoir reçu une proposition vaccinale durant la grossesse. D'autres études sur le même sujet ont retrouvé comme nous qu'un âge plus élevé et un haut niveau d'éducation étaient associés à une meilleure connaissance concernant la grippe et la vaccination antigrippale (68,69). À l'inverse de nos résultats, Mayet et al retrouvaient que la multiparité – et non la nulliparité – était associée à une meilleure connaissance des femmes enceintes (69). En ce qui concerne la proposition vaccinale par un professionnel de santé, celle-ci est apparue dans notre étude, et dans d'autres,

comme un déterminant essentiel des bonnes connaissances chez les femmes enceintes (68,69,75,93,96). En outre, 67% des participantes de notre étude ont déclaré que les professionnels de santé étaient leur principale source d'information concernant la grippe et la vaccination antigrippale (75).

Dans la dernière partie de notre travail, il paraissait ainsi logique de nous intéresser plus spécifiquement aux connaissances et aux pratiques des professionnels de santé concernant la grippe et la vaccination antigrippale pendant la grossesse. Le frein le plus fréquemment déclaré par les professionnels de notre étude était le refus fréquent des patientes. Ce résultat est concordant avec celui d'une étude réalisée en Iran et publiée en 2012, qui retrouvait que la majorité des femmes avaient refusé de se faire vacciner (84). Les principales raisons mentionnées par les femmes étaient la peur d'effets indésirables du vaccin et la perception de ne pas être à risque de complications (53,54,57,68,70,84). Les professionnels de santé de notre étude ressentaient également un manque de connaissance de leur part. Ce résultat était conforté par la revue de la littérature de Morales et al, qui retrouvaient également le manque de connaissance des professionnels comme un des plus fréquents freins rencontrés à la vaccination (83).

Il est pourtant possible que les professionnels de santé interrogés dans notre étude aient été des professionnels assez impliqués dans la vaccination antigrippale. Leur taux de réponse de 41% à notre enquête postale témoigne d'un intérêt certain pour la question. Nous avons par ailleurs noté que plus de 70% d'entre eux ont déclaré avoir été vaccinés contre la grippe au cours des 2 dernières années, ce qui est élevé en comparaison aux taux compris entre 15,6% à 63,2% retrouvés chez les professionnels de santé de différents pays européens en 2018 (80). Concernant les pratiques de ces professionnels de santé, 70% déclaraient proposer « souvent » ou

« très souvent » le vaccin contre la grippe. Cela correspond aux taux retrouvés dans les articles publiés aux États-Unis, d'après une revue de la littérature de 2020 (83).

Ces données concernant la motivation des médecins méritent cependant d'être modulées. Il est à noter en effet qu'un tiers des études qui mesurent une motivation importante des médecins à vacciner retrouvent en même temps des taux de proposition du vaccin inférieurs à 50% (83). Ceci nous amène à évoquer la possibilité d'une « dissociation » entre le niveau de connaissance concernant la grippe et la vaccination antigrippale des femmes enceintes et les pratiques réelles des professionnels interrogés. Dans notre étude en effet, les professionnels de santé ayant les meilleures connaissances n'étaient pas plus fréquemment vaccinés contre la grippe, ne fournissaient pas plus souvent le formulaire de remboursement, ne proposaient pas plus souvent le vaccin et n'avaient pas plus l'intention de se faire vacciner pendant leur(s) grossesse(s) ou celle(s) de leur compagne. Cette dissociation entre les déclarations des médecins et leurs actions réelles a été retrouvée par d'autres (83) et peut être due en partie à la sous-estimation qu'ils se font des risques de la grippe pendant la grossesse (88,89) ; à la peur d'effets indésirables du vaccin (85) et/ou à des potentiels conflits d'intérêts non avoués par l'État avec les firmes pharmaceutiques (83,87). En France en effet, le scepticisme concernant la vaccination parmi les professionnels de santé ne fait que croître depuis les années 1990 (77).

Finalement, les données de notre étude concordent entre elles, puisque la méconnaissance des complications de la grippe et de la vaccination antigrippale chez les femmes enceintes croise, dans une moindre mesure, celle des

professionnels de santé en qui elles ont pourtant confiance pour ce type d'informations. Dans une étude française datant de 2014, neuf femmes sur dix déclaraient ne pas avoir reçu suffisamment d'informations sur la grippe durant leur grossesse (70). Aux États-Unis, une autre étude montrait que 83% des femmes non vaccinées considéraient que les informations reçues par les professionnels de santé n'étaient pas suffisantes pour les convaincre de se faire vacciner, alors qu'elles auraient été prêtes à le faire si elles avaient été mieux informées (81). Dans notre étude, le lien très fort de la proposition vaccinale par un professionnel de santé et de la remise du formulaire de remboursement avec la recours à la vaccination vont dans ce sens, de même qu'une analyse récente du CDC de 2016-2017 (59). Il est vrai, cette analyse révélait des taux de vaccination de 70,5% parmi les femmes qui ont reçu une recommandation vaccinale par un professionnel de santé et à qui le vaccin a été offert ; contre 43,7% quand le vaccin était seulement recommandé et 14,8% quand le vaccin n'était ni recommandé, ni offert (53%, 35% et 2% respectivement dans notre étude).

L'ensemble de ces résultats démontre pour nous la nécessité d'instaurer des mesures pour augmenter la qualité de l'information fournie aux femmes enceintes et surtout aux professionnels de santé qu'elles consultent (54,65,83,93,94) ; d'autant que certaines études, tout comme la nôtre, tendent à montrer que les sources d'informations comme la télévision, la radio, internet, la famille ou les amis entraînent quant à elles plutôt une diminution du recours à la vaccination (57,63,64).

Conclusions :

La vaccination contre la grippe chez les femmes enceintes en France reste faible, malgré le fait qu'il s'agisse d'un problème de santé publique réel face auquel elle constitue un moyen de prévention fiable. À partir des données de ce travail et de leur croisement avec la littérature, il nous semble nécessaire pour augmenter la couverture vaccinale de mener une, voire des action(s) de santé publique à destination des femmes enceintes et surtout des professionnels de santé qui les prennent en charge. Il s'agit en effet d'améliorer leurs connaissances concernant la gravité de la maladie, l'efficacité du vaccin pour la mère et pour le bébé et sa prise en charge totale par l'Assurance Maladie. Parmi les facteurs susceptibles d'augmenter la couverture vaccinale que nous avons identifiés, ceux sur lesquels nous pouvons agir sont en effet la proposition vaccinale et la remise du formulaire de remboursement systématique à chaque femme enceinte durant la saison hivernale, associées à une information convaincue et convaincante concernant les risques de la grippe durant la grossesse, ainsi que les bénéfices de la vaccination pour la mère et le nouveau-né.

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Annexes :

- I. Annexe 1 : questionnaire destiné aux femmes enceintes

Répondre aux 4 questions PUIS si une case grise cochée à la question a) : STOP

a) Pour pouvoir participer à cette étude, nous devons connaître certaines informations :

- avez-vous plus de 18 ans ? oui non
- parlez-vous français ? oui non
- lisez-vous le français oui difficilement pas du tout
- êtes-vous allergique aux protéines de l'œuf ? non oui
- êtes-vous d'accord pour remplir ce questionnaire ? oui non

b) Quel est votre niveau d'études ?

- Primaire Secondaire ou technique Baccalauréat ou supérieur

c) Quand avez-vous débuté votre suivi de grossesse à Jeanne de Flandre ?

- 1^{er} trimestre 2^{ème} trimestre 3^{ème} trimestre

d) Quel est le nom de la personne qui vous a suivie à Jeanne de Flandre (au moins 2 fois) ?.....

1) Selon vous, la **grippe** est une maladie : (pour chaque proposition, entourez le chiffre qui correspond à votre opinion)

Très rare											Très fréquente
0	1	2	3	4	5	6	7	8	9	9	
Jamais grave											Toujours grave
0	1	2	3	4	5	6	7	8	9	9	

2) Pensez-vous que la grippe peut entraîner des **complications graves** pendant la grossesse **chez la mère** ?

- Oui Non Je ne sais pas

➤ Si oui, pouvez-vous donner un exemple ?

3) Pensez-vous que la grippe peut entraîner des **complications graves** pendant la grossesse **chez le bébé** ?

- Oui Non Je ne sais pas

➤ Si oui, pouvez-vous donner un exemple ?

4) Selon vous, la **vaccination** contre la grippe pendant la **grossesse** est :

- Contre indiquée Inutile Peut être utile Certainement utile

5) Selon vous, la **vaccination** contre la grippe pendant la **grossesse** est :

- Obligatoire Ni obligatoire, ni recommandée
 Recommandée par les autorités de santé Je ne sais pas

6) Avez-vous déjà été **vaccinée contre la grippe** ?

- Oui, en dehors d'une grossesse Non
 Oui, lors d'une précédente grossesse Je ne sais pas

7) Quelles ont été vos **sources d'information** concernant la **vaccination** contre la grippe ? (plusieurs réponses possibles)

- Professionnels de santé (médecin, sage-femme, infirmier, pharmacien...)
- Médias (radio, télévision, journaux et magazines, internet, affiches publicitaires, ...)
- Forums de discussion (Chat, associations de personnes...)
- Entourage (famille, amis...)
- Autorités officielles de santé (HAS, Inpes, Ansm....)
- Autres :

8) Parmi ces **sources**, précisez **celle** qui a motivé votre décision (se vacciner ou non) ?

TOURNEZ

9) **Au cours de cette grossesse**, vous a-t-on **proposé** la vaccination contre la grippe ?

Oui Non

➤ Si oui, qui vous l'a proposée ?

Gynécologue Obstétricien de Jeanne de Flandre Médecin généraliste

Sage-femme à Jeanne de Flandre Sage-femme libérale


Autre :

10) Pendant la grossesse, vous a-t-on remis le **formulaire de remboursement** de la vaccination par la sécurité sociale (bon de gratuité)?

Oui Non

11) Avez-vous été **vaccinée** contre la grippe au cours de **cette grossesse** ?

Oui Non Je ne sais pas

 **Si oui,**

⇒ par qui ?

⇒ à quel moment de la grossesse avez-vous effectué la vaccination ?

1^{er} trimestre (0 -3 mois) 2^{ème} trimestre (4-6 mois) 3^{ème} trimestre (7-9 mois)

⇒ quels ont été vos arguments ? (*plusieurs réponses possibles*)

Le vaccin me protège


Le vaccin protège mon bébé

J'ai reçu des informations suffisantes sur les bénéfices du vaccin

Je suis plutôt « pour » les vaccins en général

Le vaccin est remboursé intégralement

Autre :

 **Si non,**

⇒ quelles ont été vos réticences ? (*plusieurs réponses possibles*)

Je ne savais pas qu'il existait un vaccin

J'ai eu peur pour la santé de mon bébé

J'ai eu peur pour ma santé

Je n'ai pas eu assez d'informations sur les bénéfices et les risques

Je suis plutôt « contre » les vaccins

Autre :

12) Quelle **personne** vous a surtout aidée à faire **votre choix** ?

Médecin traitant Gynéco/sage-femme de ville Gynéco/sage-femme maternité Ami/famille Autre

13) Selon vous, le **vaccin** antigrippal peut entraîner, **chez la mère**, des **complications** :

(entourez le chiffre qui correspond à votre opinion)

Très rares

0 1 2 3 4 5 6 7 8 9

Très fréquentes

Jamais graves

0 1 2 3 4 5 6 7 8 9

Toujours graves

14) Selon vous, le **vaccin** antigrippal peut entraîner, **chez le bébé**, des **complications** :

(entourez le chiffre qui correspond à votre opinion)

Très rares

0 1 2 3 4 5 6 7 8 9

Très fréquentes

Jamais graves

0 1 2 3 4 5 6 7 8 9

Toujours graves

15) Si vous n'étiez pas vaccinée, **pensez-vous le faire maintenant** ?

Oui Non

UN GRAND MERCI POUR VOTRE

PARTICIPATION !

II. Annexe 2 : score de bonne connaissance

- 1) Selon vous, la **grippe** est une maladie : (*pour chaque proposition, entourez le chiffre qui correspond à votre opinion*)

Très rare Très fréquente

0 1 2 3 4 5 6 7 8 9

Si réponse <5 : 1 point

Jamais grave

Toujours grave

0 1 2 3 4 5 6 7 8 9

Si réponse <5 : 1 point

- 2) Pensez-vous que la grippe peut entraîner des **complications graves** pendant la grossesse **chez la mère** ?

Si réponse « oui » : 1 point

- 3) Pensez-vous que la grippe peut entraîner des **complications graves** pendant la grossesse **chez le bébé** ?

Si réponse « oui » : 1 point

- 4) Selon vous, la **vaccination** contre la grippe pendant la **grossesse** est :

Si réponse « peut être utile » : 0,5 point

Si réponse « certainement utile » : 1 point

- 5) Selon vous, la **vaccination** contre la grippe pendant la **grossesse** est :

Si réponse « obligatoire » : 0,5 points

Si réponse « recommandée » : 1 point

- 13) Selon vous, le **vaccin** antigrippal peut entraîner, **chez la mère**, des **complications** :

(*entourez le chiffre qui correspond à votre opinion*)

Très rares

Très fréquentes

0 1 2 3 4 5 6 7 8 9

Si réponse 5, 6, 7 : 1 point

Jamais graves

Toujours graves

0 1 2 3 4 5 6 7 8 9

Si réponse <3 : 1 point

- 14) Selon vous, le **vaccin** antigrippal peut entraîner, **chez le bébé**, des **complications** :

(*entourez le chiffre qui correspond à votre opinion*)

Très rares

Très fréquentes

0 1 2 3 4 5 6 7 8 9

Si réponse <3 : 1 point

Jamais graves

Toujours graves

0 1 2 3 4 5 6 7 8 9

Si réponse <3 : 1 point

III. Annexe 3 : questionnaire destiné aux professionnels santé

ETUDE GESTAGRIP : QUESTIONNAIRE POUR LES PROFESSIONNELS Code GG _____

- 1) Vous êtes : un homme une femme
- 2) Vous êtes : sage-femme médecin
- 3) Vous exercez depuis : moins de 5 ans 5 à 15 ans plus de 15 ans
- 4) Avez-vous déjà eu la grippe ? oui non
- 5) La grippe est une maladie : (*pour chaque proposition, entourez le chiffre qui correspond à votre opinion*)
- | | | | | | | | | | | |
|-----------------|---|---|---|---|---|---|---|---|---|-------------------------|
| Très rare | | | | | | | | | | Très fréquente |
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | |
| Jamais grave | | | | | | | | | | Toujours grave |
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | |
| Non contagieuse | | | | | | | | | | Extrêmement contagieuse |
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | |
- 6) Le risque de mortalité lié à la grippe chez une femme enceinte est :
- nul multiplié par 5 multiplié par 15 je ne sais pas
- 7) Quelles sont les recommandations concernant la vaccination antigrippale pendant la grossesse ?
- non recommandé
- recommandé quel que soit l'âge gestationnel
- recommandé au 1^{er} trimestre de grossesse
- recommandé au 2^{ème} trimestre de grossesse
- recommandé au 3^{ème} trimestre de grossesse
- 8) Le vaccin antigrippal injectable est-il un vaccin viral vivant ?
- oui non je ne sais pas
- 9) Après vaccination, à combien estimez-vous le taux de protection vaccinale antigrippale ? (*entourez le chiffre qui correspond à votre opinion*)
- | | | | | | | | | | | |
|----|---|---|---|---|---|---|---|---|---|------|
| 0% | | | | | | | | | | 100% |
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | |
- 10) Selon vous, les effets secondaires du vaccin antigrippal dans la population générale ou bien chez la femme enceinte sont-ils ? (*une seule réponse possible*)
- graves et fréquents non graves et fréquents
- graves et non fréquents non graves et non fréquents
- 11) Le cas échéant, précisez l'effet secondaire qui vous gêne le plus chez la femme enceinte :
-
-
- 12) Selon vous, les effets secondaires du vaccin antigrippal chez le fœtus sont-ils ? (*une seule réponse possible*)
- graves et fréquents non graves et fréquents
- graves et non fréquents non graves et non fréquents
- 13) Le cas échéant, précisez l'effet secondaire qui vous gêne le plus chez le fœtus :
-
-
- 14) Vous proposez la vaccination antigrippale chez la femme enceinte en consultation prénatale : (*entourez le chiffre qui correspond à votre opinion*)

Jamais 0 1 2 3 4 5 6 7 8 9 Systématiquement

15) Délivrez-vous aux patientes le formulaire de la Sécurité Sociale dédié à la gratuité de la vaccination antigrippale chez la femme enceinte ? *(une seule réponse possible)*

- oui non je ne le connais pas

16) Si vous le connaissez, ce formulaire vous paraît-il : *(pour chaque item, cocher la réponse qui vous correspond)*

- utile Oui Non
- pratique Oui Non
- facile à expliquer aux patientes Oui Non
- compréhensible par les patientes Oui Non
- autre :

.....

17) Quels sont les freins que vous avez éventuellement rencontrés à la vaccination antigrippale chez la femme enceinte ? *(plusieurs réponses possibles)*

- manque de temps
- manque d'informations/de connaissances
- je n'adhère pas aux recommandations
- la balance bénéfice/risque me paraît insuffisante
- refus fréquent par les patientes
- autres :

.....

18) A quelle fréquence rencontrez-vous ces freins dans votre pratique ? *(entourez le chiffre qui correspond à votre opinion)*

Jamais 0 1 2 3 4 5 6 7 8 9 Tout le temps

19) Par quelle(s) source(s) avez-vous été informé(e) pour toutes ces données concernant la grippe ? *(plusieurs réponses possibles)*

- sources officielles de santé (HAS, ANSM, HCSP, CTV, ARS...)
- confrères, réunions de service
- médias
- autres :

.....

20) Si vous étiez enceinte, feriez-vous la vaccination antigrippale au cours de la grossesse ? (si c'était votre conjointe, lui conseilleriez-vous ?)

- oui non

21) Avez-vous été vacciné(e) contre la grippe au cours des deux dernières années ?

- oui non

22) Avez-vous des propositions pour améliorer la couverture vaccinale antigrippale chez la femme enceinte ?

.....
